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Archives of Neurology and Psychiatry

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PAPILLOMAS OF THE CHOROID PLEXUS

WITH THE REPORT OF SIX CASES *

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Though the pathologic diagnosis of intracranial tumors may often be made with considerable accuracy at the time of operation from their gross appearance alone, the subsequent histologic study of the tissues not infrequently controverts the provisional diagnosis thus made, for the cellular architecture of many of these lesions often reveals peculiarities previously unsuspected. However, a proper histologic examination must comprise much more than the routine hematoxylin and eosin stains which may serve merely to add confusion to a classification supported by the gross appearance of the lesion. One of us (Cushing) has pointed out that this is true, for example, of the common tumors (neurinomas) of the lateral recess, the great majority of which arise from the nervus acusticus.

Consequently, if we are to rely on a histologic diagnosis for tumor classification, it is necessary to lean on something more dependable than the mere architectural arrangements of the cells, and this is provided by the chemical affinity which the cells of different types or portions of them possess for special dyes. Thus in this clinic it has been possible for Bailey [1] to separate from the gliomas, with which they had previously been confused, the group of tumors which arise from the ependymal cells; for, regardless of the general appearances shown on section, the blepharoplasten of the cells composing a true ependymoma apparently occur in no other tumors (except the pinealomas), and when stained and recognized the growth can be mistaken for no other.

* From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston.
* Presented before the American Neurological Association, Philadelphia, June 7, 1924.

1. Bailey, Percival: A Study of Tumors Arising from Ependymal Cells, Arch. Neurol. & Psychiat. **11**:1-27 (Jan.) 1924.

This communication will be given over to a consideration of the equally rare tumors arising from the choroid plexus. Whereas many of these papillomatous or cystic tumors are unmistakable to the naked eye and others easily identified by the microscope, for want of proper study, a variety of lesions which lie in the proximity of the lateral and fourth and even the third ventricles have been confused with them. In the course of certain studies of the choroid plexus,[2] Bailey and Davis have shown that the cells are rich in mitochondria while blepharoplasten are absent, and it is believed that these findings will be of value in the more accurate diagnosis of the growths which actually take their origin from the plexus.

THE MORPHOLOGY OF THE PLEXUS

The choroid and ependymal cells of man have a common origin, and their differentiation occurs rather late. In the development of the plexuses, the ventricular ependyma becomes thickened, differentiates and invaginates. It then gradually becomes tufted and projects into the ventricles. The true ependymal cells lie adjacent to a very dense layer of fibrillary glia designated as the subependymal glia. The choroid cells, on the other hand, lie on a connective tissue stroma which contains an uncommonly rich network of blood vessels.

According to Meek,[3] in many animals, as the guinea-pig, mouse and rat, the plexuses consist of smooth laminae without villi, whereas villi are abundant in the plexuses of the horse, ox, crocodile, some of the selachians and in man. The principal arteries and veins supplying the plexus run longitudinally along its base. The arteries branch repeatedly until a very close capillary network is formed. This is best marked at the surface of the plexus immediately beneath the epithelium. Each of the larger villi contains an afferent artery and efferent veins. Some of the arteries have thick walls and possess a narrow lumen, while others have a wide lumina, resembling sinuses, and the walls are composed of white fibrous connective tissue which cannot be differentiated into intima, media and adventitia.

All observers are in accord in stating that in accurately cut sections the covering epithelium of the villi consists of a single layer of cuboidal cells. In living tissue the cytoplasm of these cells is finely granular and has a homogeneous structure. It is limited on its free side by a cuticular membrane which in animals gives insertion to ciliae. For a short time in

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2. Bailey, P., and Davis, L. E.: A Progressive Staining Method for Mitochondria, J. Med. Res. **44**:535-537 (Sept.) 1924. Davis, L. E.: A Physio-Pathologic Study of the Choroid Plexus with the Report of a Case of Villous Hypertrophy, ibid. pp. 521-534.

3. Meek, W. J.: A Study of the Choroid Plexus, J. Comp. Neurol. & Psychiat. **17**:286, 1907.

the embryonic life of man, the choroid cells are ciliated, and at the base of each cilium is a small body known as a "blepharoplast." This may consist of a single granule, a pair of granules lying one above the other, a minute bacillus-like rod, or it may have the form of a dumb-bell. In the human adult choroid cell, however, the "blepharoplasten" have disappeared, and as they persist in the adult ependymal cells, this fact serves as a precise means of differentiation.

During the development of the choroid cells, their cytoplasm becomes more granular, and the round or oval nucleus comes to lie in the basal zone. In fixed sections of the human plexus, many large, round, coarse granules may be seen to fill the entire cell body and to have a tendency to be arranged perinuclearly. These granules, which have been regarded by many as an indication of the secretory activity of the cells, can best be demonstrated in material fixed in Regaud's fluid or in formalin-fixed material which has been mordanted in 3 per cent. potassium bichromate. In tissues thus fixed, the granules are very easily stained by Mallory's phosphotungstic-acid-hematoxylin or by Cowdry's anilin-fuchsin-methyl-green methods. The granules, moreover, are identical in their staining reactions with the mitochondria found in other living cells, and there is no evidence for assigning to them a secretory function such as is attributed to the zymogen granules of the pancreas. In addition to these granules, the cell protoplasm is often seen to contain what are described as vacuoles. These spaces, as shown by Ciaccio and Scaglione [4] and by Askanazy,[5] contain a lipoid substance which plays no part so far as we know in the cell physiology. Askanazy has also pointed out that in embryonal life the cells contain demonstrable glycogen, which, however, is absent in postnatal life.

BIBLIOGRAPHY OF PLEXUS TUMORS

The literature on the subject is characterized by a tendency to describe in one category a great variety of lesions which protrude into the ventricles, and to assume, without accurate histologic evidence, that they actually have originated from the adjacent plexus. Many of the early papers on the subject deal with primary epithelial tumors of all sorts which are found in the brain and consequently include such diverse lesions as the rare epidermoid cholesteatomas and the fairly common suprasellar cysts lined by squamous epithelium which originate from reliques of Rathke's pouch, and which have become well understood only of late years. These are easily recognized even in the somewhat

4. Ciaccio, C., and Scaglione, S.: Beiträge zur cellular Physiopathologie der Plexus chorioidei, Beitr. z. path. Anat. u. allgem. Path. **55**:131, 1913.

5. Askanazy, M.: Zur Physiologie und Pathologie der Plexus chorioidei, Verhandl. Deutsch. path. Gesellsch. **17**:85-103, 1914.

indefinite descriptions of the lesions which are apt to be given; but the identification of the other tumors included in these early papers is more difficult.

One of the most frequently quoted articles on the subject of these primary epithelial tumors is that by Boudet and Clunet [6] published in 1910 from Pierre Marie's laboratory. These authors assembled from the literature thirty-six cases of the most varied sort and added two observations of their own. Only the first of their cases, however, appears to be a true papilloma arising from the lateral plexus; the other is unmistakably a pharyngeal pouch tumor giving "une image rappelant de très près la couche basale des épithéliomas adamantins." However, as the title of their article indicates, these authors made no pretense of limiting their study solely to the true plexus tumors, and in their thirty-six listed cases taken from the literature, only thirteen fairly undoubted examples occur. These in our estimation are as follows: the cases by Guérard, 1833; Robin, 1858; Chouppe-Verron, 1874; [7] Demange, 1874; Curschmann, 1877; Douty, 1885; Audry, 1886; Brüchanow, 1898; Bielschowky and Unger, 1906; Dobson, 1907; Vigouroux, 1908; Rossbach, 1909; Slaymaker and Elias, 1909.[8] Even from the brief descriptions of the other twenty-three cases, it is apparent that a great many of them cannot be the tumors in question; and the doubtful cases on consulting the original sources prove to be lesions of the following types: perithelioma, ependymoma, craniopharyngeal pouch cyst, meningioma, cholesteatoma, together with other obscure growths which are unillustrated and the nature of which cannot be definitely made out from the descriptions.

This pursuit we have found a most baffling one. It has served at least to show the great need of a more exact differentiation of these

6. Boudet, C., and Clunet, S.: Contribution à l'étude des tumeurs epéthéliales primitives de l'encéphale, développées aux dépens des formations épendymaires et particulièrement des plexus choroïdes, Arch. de méd. expér. et d'anat. path. **22**:379-411, 1910.

7. This typical example of a papilloma of the fourth ventricle found at necropsy in a man 42 years of age was the basis of Verron's Paris Thesis, 1874 (Étude sur les tumeurs du IV. ventricule). This thesis gives a brief account of nineteen additional examples of fourth-ventricle tumor, only two of which appear to be papillomas of the plexus; the case by Robin which Boudet and Clunet included, and another briefly reported by Garrod (The Lancet, 1873, March, p. 303) which for some reason or another they excluded. Verron's cases have been quoted in the subsequent literature.

8. To these early cases should be added the case demonstrated by Stroeber in 1893 (Berl. klin. Wchnschr. **30**:123, 1893) before the Berlin Medical Society, viz., a papillary and epithelial-lined tumor growing from the plexus of the lateral ventricle in the brain of a child 18 months of age; also the probable case reported by Paul Süttgen in 1896 (Maug.-Diss., Würzburg).

obscure and rare lesions. As it is our purpose to limit the discussion to the true papillomas of the plexus, the still more infrequent tumors, such as the so-called cholesteatoma of the plexus (really an endothelioma),[9] the perithelial angiosarcoma,[10] etc., of which no examples occur in our series, will be left out of consideration. The tumor above all others for which the papillomas of the plexus are most likely to be mistaken is the papillary ependymoma which tends to seed itself, like certain papillomas elsewhere in the body, and to show multiple foci of growth.[11] So far as we are aware, the choroid plexus tumors, on the other hand, remain single. However, the two can be clearly differentiated by the fact, first clearly emphasized by Saxer,[12] that the core of the papillae of the ependymal papilloma is composed of subependymal glia,[13] whereas the core of the plexus tumors is connective tissue.

Moreover, the mitochondria of the ependymal epithelium are scanty and minute, whereas those of the plexus epithelium are abundant and coarsely granular. Another differential point is the absence of blepharoplasten in the cells of the plexus epithelium.

Since Boudet and Clunet's paper in 1910, the literature on the subject has been meager, and the titles of the few published papers misleading. Doubtless many case reports may be hidden in articles dealing with the subject of brain tumors in general or tumors of special areas like those of the fourth ventricle and are not traceable through the indexes. Moreover, the ever present difficulty of determining from the author's description the exact histologic nature of the lesion is an additional handicap in the pursuit of the subject. Possible examples are

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9. Blumer, George: Bilateral Cholesteatomatous Endotheliomata of the Choroid Plexus, Johns Hopkins Hosp. Rep. (Welch Festschrift), 1900, pp. 279-290.

10. Borchers, Eduard: Tumoren des Plexus choriodeus des Gehirns, Maug.-Diss., München, 1909.

11. The question as to whether these tumors are ever carcinomatous in character has been dealt with by Karl Hart (Ueber primäre epithelial Geschwülste des Gehirnes, Arch. f. Psychiat. u. Nervenh. **47**:739-771, 1910), who states that the literature contains record of only two examples of primary epithelial growths which had carcinomatous characteristics. These are the cases of Späts and of Kölpin. The matter is obscure.

12. Saxer, F.: Ependymepithel, Gliome und epitheliale Geschwülste des Centralnervensystems, Beitr. z. path. Anat. u. Path. **32**:276, 1902.

13. Only one of the recognized ependymomas in our own series, now thirteen in number, eight of which arose from the fourth ventricle, showed evidence of papillary formation, all being solid tumors. A good example, however, of the papillary ependymoma has been reported by Linck in Ziegler's Beiträge **23**:98, 1903. It must be an exceedingly rare lesion in its papillomatous form which represents an early stage of growth such as might be brought to view as an accidental postmortem finding.

the cases reported by Weygandt [14] (1917), by Goodhart [15] (1918), and by Lorenzini [16] (1922), though the cystic lesion Lorenzini describes and illustrates is a peculiar one, and we are uncertain of its nature not only from the description but from the fact that it was located in the third ventricle, a rare seat for these plexus tumors.[17]

With the case of Perthes [18] reported in 1919 begins the surgical literature on the subject. But doubts may be cast on the propriety of including Perthes' case, for the reason that it is histologically reported to be an endothelial sarcoma, though mentioned elsewhere in the text as being a papillary tumor arising from the plexus of the lateral ventricle (it involved the occipital lobe and was visible on the surface of the brain). However this may be, an undoubted plexus papilloma of the fourth ventricle has been successfully operated on by Ernest Sachs [19] (1922) with removal of the tumor. The case unfortunately was reported purely from its neurosurgical aspects, and the author neglected to give a histologic description of the lesion. It proves, however, microscopically to be a typical true papilloma of the plexus.

It would appear from the description of the cases in the literature as well as from our own experience that the tumors arising from the plexus of the fourth ventricle are more apt to be unmistakable to the naked eye from their papillary appearance than are those of the lateral ventricle which are apt to be enveloped by cysts. Accompanying the case report by Slaymaker and Elias,[20] which was included in Boudet and Clunet's series, is the best illustration in the literature of one of these large fourth ventricle lesions in situ. It is of precisely the same sort as that encountered in Case 1 and Case 6 of the present series and per-

14. Weygandt: Hydrozephalus mit Tumor (Papillom des Plexus chorioideus), Deutsch. med. Wchnschr. **43**:797, 1917.

15. Goodhart, G. W.: Adenoma of the Choroid Plexus, Guy's Hosp. Rep. **69**:219-222, 1918.

16. Lorenzini, Aldo: Papilloma cistico del terzo ventricolo, Riv. di clin. pediat., Firenze **20**:705-749, 1922.

17. Another case has come to light in Ribbert's Geschwulstlehre, 1904, p. 359. Rheindorf reported another in the Charité-Annalen **32**:294, 1908. Natonek gives a particularly well described example in Virchow's Arch. f. Path. Anat. **218**:170, 1914.

18. Perthes: Glückliche Entfernung eines Tumors des Plexus chorioideus aus dem Seiten Ventrikel des Cerebrum, München. med. Wchnschr. **66**:677-78, 1919.

19. Sachs, Ernest: Papilloma of the Fourth Ventricle: Report of a Case, Arch. Neurol. & Psychiat. **8**:378-382 (Oct.) 1922.

20. Slaymaker, S. R., and Elias, F.: Papilloma of Choroid Plexus with Hydrocephalus, Tr. Chicago Path. Soc. **7**:187-195, 1907-1909; Arch. Int. Med. **3**:289-294 (May) 1909.

mission to include a photograph has been kindly given by Dr. Le Count of Chicago in whose collection of brain tumors the specimen remains (Fig. 1).

PERSONAL OBSERVATIONS

In a series of 964 cases of verified brain tumors, neoplasms, which beyond any reasonable doubt have arisen from the choroid plexus, have been encountered in only six instances. Of these, two tumors were apparently associated with the plexus of the lateral ventricle and four with the plexus of the fourth ventricle. Two other cases which had been indexed as presumable tumors of the plexus have been excluded on the

Fig. 1.—Large papilloma arising from the tela choroidea of the fourth ventricle (natural size). Case of Slaymaker and Elias.

grounds of uncertainty. One is a multicystic epithelial tumor of the lateral ventricle not papillary in character. The other appears in all probability to be a metastatic papillary tumor.

The material of the six accepted cases had been fixed in 10 per cent. formalin in three instances whereas in three others only Zenker-fixed tissue was available for study. While the latter fixative makes it possible to use stains suitable for the display of the general architecture of the lesion, it precludes the employment of many special staining methods helpful in determining the exact nature of the cells. On formalin-fixed material it is possible to mordant the tissue in 3 per cent. potassium bichromate solution and then to employ various differential cytologic

methods. In our studies, hematoxylin and eosin, phosphotungstic acid-hematoxylin, ethyl violet-orange G, van Gieson's, Mallory's connective tissue and Cowdry's mitochondrial stains have been used.

In the case histories which follow it will appear that in only one instance (Case 2) was the lesion first brought to view at necropsy so that its exact anatomic relations unaffected by operative interference could be subjected to study. However, in all the other cases but one (Case 3) the source of origin was sufficiently clear. We are naturally interested in three separate aspects of these cases: their diagnosis and localization, their operability, their gross and histopathologic aspects. Each of these will be touched on in commenting on the case reports. The first two cases are from the records of the senior author while at the Johns Hopkins Hospital.

CASE 1.—*Suspected cerebellar lesion. Repeated suboccipital explorations with negative findings. Ultimate identification and removal of a papillary tumor from the left cerebellar hemisphere with fatality. Tumor of the lateral choroid plexus of the fourth ventricle.*[21]

July 17, 1908.—Transfer from the medical service of Clayton S., a farmer, aged 22, who had entered the hospital with the complaint of headaches and weak eyes.

Clinical History.—For four months, the patient had noticed that stooping produced pain in the right temporal region. Two months later, he began to have spells of dizziness and faintness. At this time, he first noticed that vision was hazy, and for a few weeks before his admission there had been mild diplopia. He had lost 24 pounds (10.9 kg.) in weight.

Neurologic Findings.—Bilateral choked disk of 3 diopters. Diplopia was present for objects at a distance of 10 feet or more. There was rotary nystagmus on looking upward and lateral nystagmus on looking to either side, more marked to the left. Weakness of the left side of the face was apparent. Hearing was unaffected. There was distinct unsteadiness of position with a positive Romberg sign, and the patient carried his head tilted to the right.

Operation (July 17, 1908).—Although a tentative diagnosis of subtentorial lesion was made, it was thought that the symptoms were insufficient to warrant suboccipital exploration, and a left subtemporal decompression to relieve the intracranial tension was performed.

Clinical Course.—There was subjective improvement in vision with subsidence, though not complete disappearance, of the choked disks. The patient was discharged on Aug. 8, 1908. He returned two months later owing to increase of cerebellar symptoms, though his general condition was excellent and he had gained 20 pounds (9 kg.) in weight. The decompression was full; the choked disks measured 2.5 diopters. The nystagmus was more marked than before, especially to the left. The left facial weakness remained unchanged. An exploration of the cerebellum was advised.

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21. Case previously reported in discussing differential diagnosis of tumors of the lateral recess (Cushing, H.: Tumors of the Nervus Acusticus, Philadelphia, W. B. Saunders Company, 1917, Case XXXV, p. 226). In this article a photograph of the smooth outer surface of the tumor was reproduced.

Second Operation (Oct. 8, 1908).—A suboccipital operation was performed. No lesion was disclosed in either recess or on puncture. He made a satisfactory recovery. There was subsidence of the choked disks to 1 diopter, but his cerebellar signs remained unaltered, even to the characteristic tilting of his head, at the time of his discharge on Nov. 3, 1908 (Fig. 2).

Clinical Course.—For a year, he led a fairly comfortable life, was able to work and remained in good general condition in spite of the definite progress of his cerebellar symptoms. Their increase in severity led him to reenter the hospital.

Fig. 2 (Case 1).—Characteristic tilting of patient's head. Note protrusion of previous subtemporal decompression.

Third Operation (Nov. 11, 1909).—The cerebellum was reexplored without finding any definite pathology aside from an abundance of cerebrospinal fluid which escaped from some cystic spaces in the left recess. No tumor was disclosed.

Clinical Course.—The patient stood this disappointing exploration very well, and was discharged on Dec. 1, 1909. During the ensuing six months, his general condition remained good. He reported, July 28, 1910, having walked three miles to the station that morning. He was still able to do light work on the farm. There was no increase in his headaches or ataxia, although he deviated to the left in walking. He returned again, Oct. 10, 1910, when the left cerebellar symptoms were found to be still more pronounced. The most marked feature was constant rotary nystagmus. Professor Sänger of Hamburg saw the patient at this time, called attention to an hyporeflexa cornealis on the left, and urged further exploration of the recess.

Fourth Operation (Oct. 21, 1910).—The cerebellum and lateral recesses were again exposed. On evacuation of fluid, there was no apparent tension. No tumor was disclosed in the angle, though the seventh and eighth nerves were not brought into view. Several exploratory punctures to a 5 cm. depth met no resistance and provoked no bleeding.

Clinical Course.—For several months the patient felt improved, but at the end of this time he began to suffer for the first time from suboccipital discomforts, developed bilateral tinnitus, and his unsteadiness and ataxia had become still more pronounced. There was slight return (about 1 diopter) of choked disk. Any further exploration seemed futile, but his insistence that he had always gained temporary relief, taken with the belief that a tumor of some benign sort must certainly be present, led to his readmission.

Fig. 3 (Case 1).—Gross specimen at operation (natural size). Laterally placed papilloma of plexus quarti ventriculi lateralis removed from the left cerebellar hemisphere in which the lesion was imbedded.

Fifth Operation (Oct. 24, 1911).—The left half of the original suboccipital wound was reexplored. The left cerebellar hemisphere was incised, and at a depth of 1 cm. a soft, reddish, papillomatous tumor was found almost replacing the hemisphere. The tumor proved to be enucleable, and all but a small fragment of its attachment at the base was removed (Fig. 3). The wall of the cavity was smooth and glistening, showing that the tumor was unattached.

After a stormy postoperative period characterized by difficulty in swallowing and a high pulse rate and temperature, the patient died of pneumonia six days later, with consolidation of the right lung.

Pathologic Notes.—Examination of the brain disclosed a fragment of tumor attached to the left side of the medulla and lying in the bottom of the large cavity in the cerebellum left by the removal of the tumor. The medulla was greatly compressed laterally, and the floor of the fourth ventricle was a long

sickle-shaped groove instead of a shallow, saucer-like depression. The left inferior cerebellar peduncle followed along the bed of the tumor and passed anterior to it in the region of the dentate nucleus. The tumor appeared to have arisen from a tuft of choroid plexus in the region of Luschka's foramen. The growth removed at operation on its torn surface (Fig. 3) was soft, papillomatous and spongy. Its other intact side presented a smooth, glistening, slightly vascularized surface.

Microscopically, the formalin-fixed tumor tissue showed a papillomatous structure comprised of numerous cauliflower-like villi, which had a central core of loose white fibrous connective tissue, rather sparse in amount (Fig. 4). Many thin-walled blood vessels abounded throughout the tissue. The epithelial

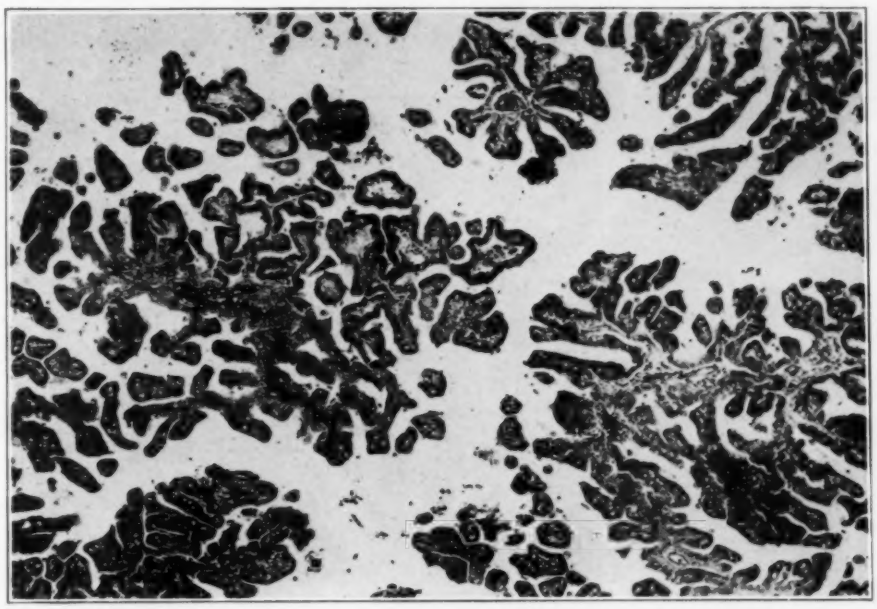


Fig. 4 (Case 1).—Papillomatous character of the growth. (Phosphotungstic acid-hematoxylin stain; × 80.)

cells covering the villi were cuboidal in shape and were arranged in one layer. The cytoplasm stained lightly and was finely granular. The nuclei were quite round, and centrally situated. Numerous concentric lamellated calcareous deposits were present throughout the tissue. The cytoplasm in the basilar portion of the cells contained very small, round, darkly stained granules which could be seen by the Cowdry and phosphotungstic acid-hematoxylin methods. These granules did not stain by the ethyl violet-orange G method. The cells did not contain "blepharoplasten," and glia fibers were not present (Fig. 5).

Comment.—In the sixteen years since this patient first came under observation, so much progress has been made in the diagnosis and operative treatment of brain tumors in general that it is difficult to

project one's self back into the state of mind of those days. Certainly, from our present standpoint, the localizing symptoms were sufficiently clear to have justified a suboccipital exploration as a primary step, with transection of the left cerebellar hemisphere had no lesion been exposed in the cerebellopontile angle. The absence even of partial deafness from the syndrome we now know to be enough to exclude the common tumor of the lateral recess, but our knowledge of the acoustic neurinomas at that time was still meager. It was on this basis of differential diagnosis that this case has been previously reported.

From a pathologic standpoint, the tumor represents the pure type of papilloma of the plexus, and even the gross appearance of the lesion which shelled out of a smooth-lined cavity left no doubt of its nature

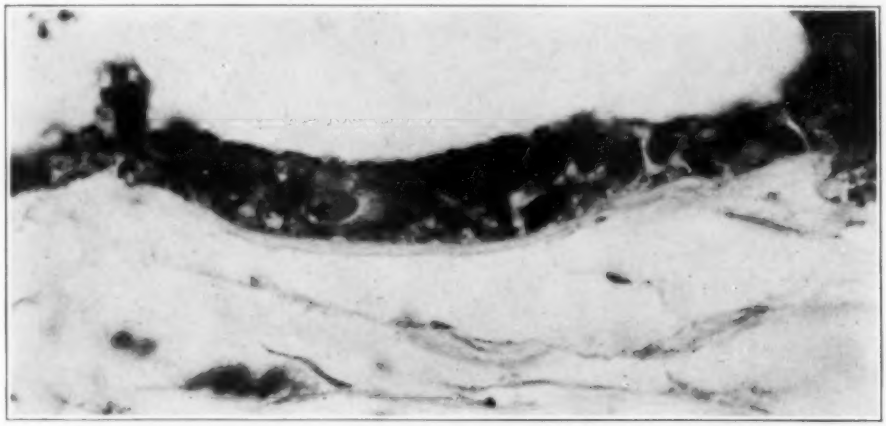


Fig. 5 (Case 1).—Coarse round granules in the epithelial cells lining the papillae of the tumor. (Anilin fuchsin-methyl green stain; × 850.)

and its benign characteristics. The point of attachment of the growth at the site of the dislocated and compressed medulla leaves no uncertainty as to its point of origin. No other example of a tumor so definitely originating from this source has been found in the literature, for most of the simple papillomas of the fourth ventricle, as will be seen, are median, not lateral, in their position. Nor does any reported papilloma of the posterior fossa appear to have reached such large dimensions. Accommodation for its increase in size for three years was undoubtedly afforded by the suboccipital decompression, and the effects of the inevitable hydrocephalus were in a measure offset by the subtemporal procedure.

CASE 2.—*Solid papillomatous tumor of posterior end of left lateral choroid plexus lying chiefly in occipital lobe and enveloped by cysts. Erroneous localization. Suboccipital exploration. Early fatality. Necropsy.*

Jan. 22, 1909.—Transfer from the medical service of William W., a boy, aged 9 years, complaining of loss of vision, headaches and vomiting.

Clinical History.—Symptoms began ten months before admission, with periodic severe general headaches, which later became almost entirely frontal in character. They were often worse at night, and were accompanied by nausea and vomiting. Of late, in association with enlargement of the head, these symptoms have become less severe. This relief of pressure unfortunately came too late to save vision. Soon after the onset of the headaches, dimness of vision was complained of; this progressed rapidly, and for six months he had been completely blind (no history of hemianopsia obtained).

Fig. 6 (Case 2).—Enlarged head and dilated extracranial vessels. Photograph after negative suboccipital exploration.

There have been two generalized convulsive seizures. The first occurred about a month after the onset of symptoms, the second some time later. He complained much of stiffness of the neck and of pain in the coccygeal region. There was also a slight loss in sense of smell and perhaps some disturbance in hearing. The child stated that early in his illness he felt as though he were upside down or "twirling around," but apparently there was no unsteadiness in gait.

Neurologic Findings.—The head was large and the cranial sutures widely separated. There was a pulsating spurious meningocele in the mid-vertex. The extracranial blood vessels were much dilated in the frontal and temporal regions. There were bilateral choked disks with secondary atrophy. There

was sustained nystagmus when the patient looked to the left, and his gait was ataxic, with a tendency to deviate to the left. Hearing was less acute on the left side. A diagnosis of left intracerebellar tumor with hydrocephalus was made.

Operation (Jan. 25, 1909).—A suboccipital exploration was performed without disclosing the lesion.

Postoperative Course.—The wound healed perfectly (Fig. 6), but the child remained dull and stupid, with no relief of symptoms. On February 1, a second operation was undertaken, in an effort to offset the internal hydrocephalus by ventricular drainage. He went from bad to worse, and on February 9, the cerebellum was again explored, with negative findings. He died six days later.

Necropsy.—The cranial sutures were all widely separated. The brain weighed approximately 2.2 kg. The left side of the tentorium cerebelli was so far pressed downward as to compress and flatten the left cerebellar hemisphere. A series of coronal sections (Fig. 7) was made. The first through

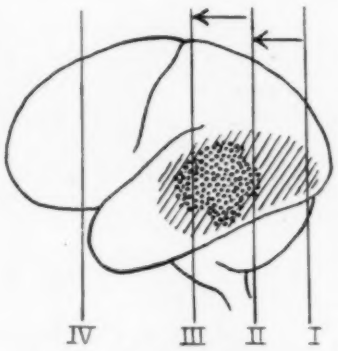
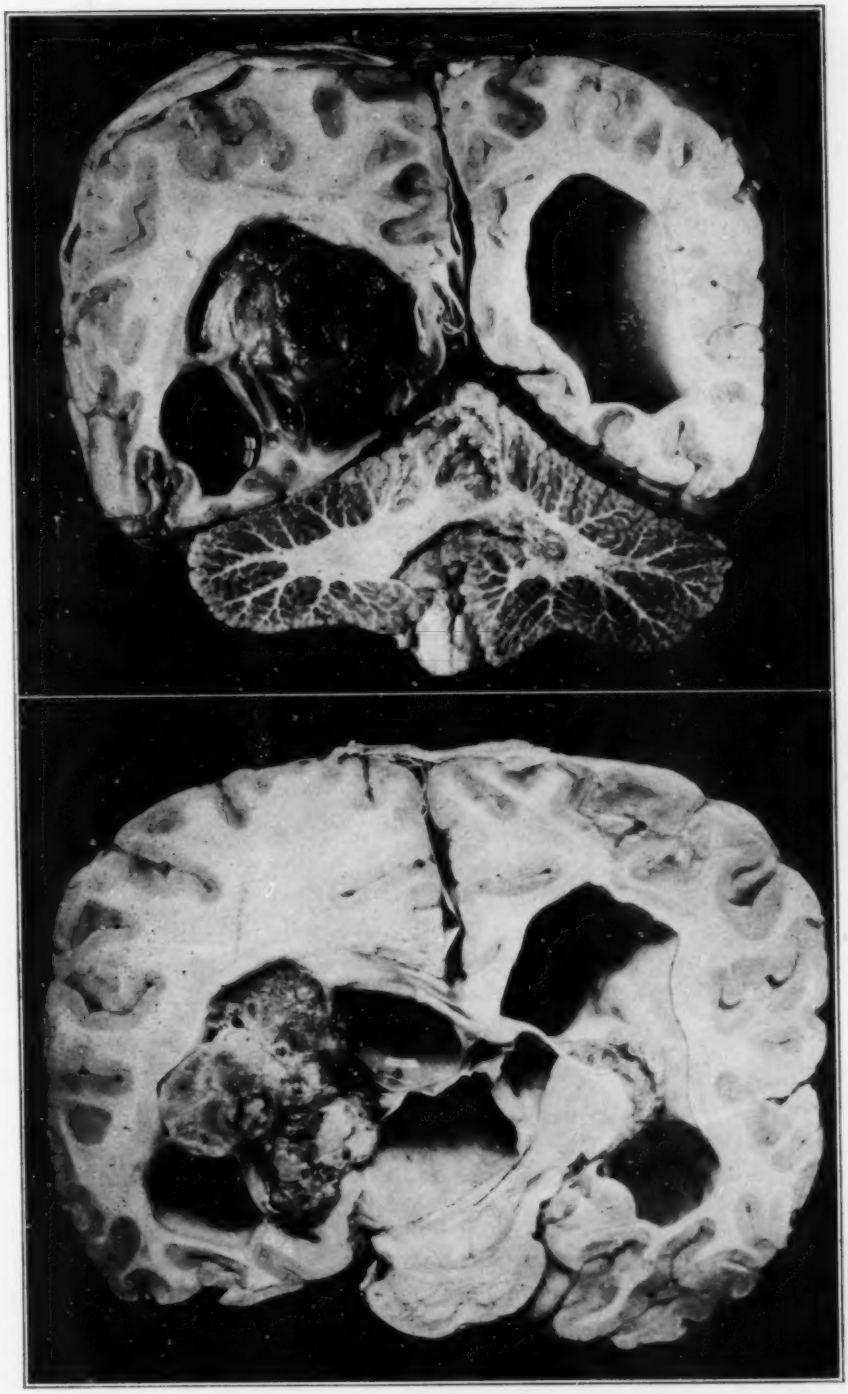


Fig. 7 (Case 2).—Orientation sketch for Figures 8 and 9, showing approximate situation of tumor mass and its enveloping cysts deep in the left occipitotemporal lobe. Arrow points to sections shown.

the tips of the occipital lobes revealed a large cystic cavity in the left hemisphere, which contained gelatinous material. A section farther forward through the center of the cerebellum (Fig. 8) disclosed a widely dilated right ventricle. In the left cerebral hemisphere, the section passed through the posterior pole of a lobulated tumor the size of a hen's egg and grayish red. The tumor was surrounded by a number of cystic cavities of variable size which contained yellowish cloudy fluid and were lined by a smooth membrane. A third section further forward (Fig. 9) through the center of the pons showed the pons to be greatly deformed, with the iter flattened and obliterated. This section transected the solid tumor and revealed a large number of cystic spaces about the growth and extending well across the median line. Other sections revealed at the upper margin of the tumor a number of blood vessels, which could be traced forward to the left choroid plexus. This plexus was pale and small in comparison with the injected and hyperemic plexus on the right. The frontal poles of both ventricles were symmetrically dilated, and the foramina of Monro were greatly enlarged.



Figs. 8 and 9 (Case 2).—Showing from the posterior aspect two views of the cyst-enveloped tumor and dilated right ventricle. Note in lower figure the marked pontile deformation.

Pathology.—The tumor showed histologically the characteristic appearance of having originated from the choroid plexus. The villi were arranged in a somewhat compact fashion, and only in places showed typical papillomatous characteristics (Fig. 10). They consisted of a very small central core of loose white connective tissue, in which were situated blood vessels. Each villus was clothed by a single layer of cuboidal cells containing a lightly stained cytoplasm and a central round nucleus. Phosphotungstic acid hematoxylin and anilin fuchsin-methyl green stained round, coarse granules which were present in the cytoplasm (Fig. 11). These were not so numerous as those which were found in the normal plexus cells, and were much smaller in size. Their staining characteristics were identical, however. Ethyl violet-orange G did not stain these granules. Many cells contained quite large clear vacuoles.

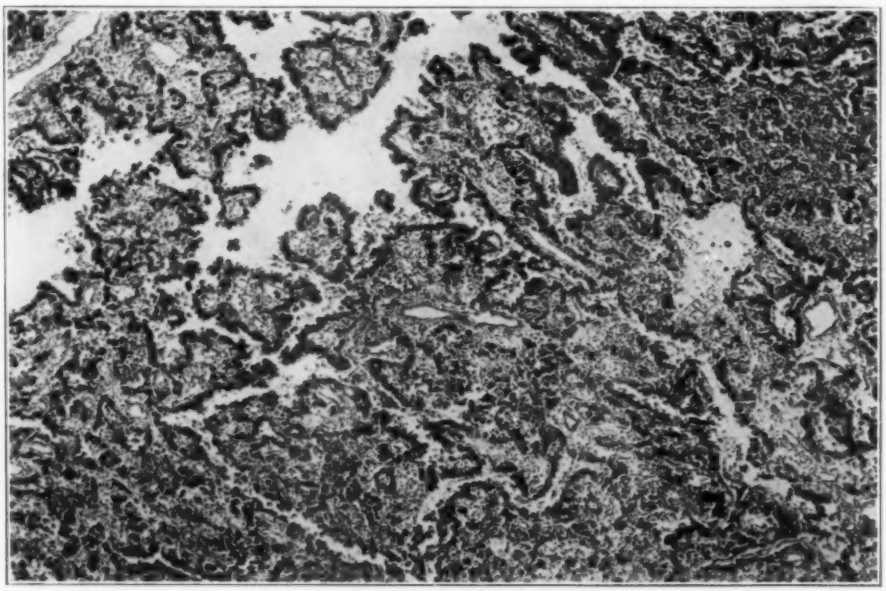


Fig. 10 (Case 2).—Showing the papillomatous nature of the growth (van Gieson; × 80).

Mallory's connective tissue stain and van Gieson's stain showed a very small amount of loose white fibrous tissue between the villi. Corpora amylacae were present and showed a characteristic concentric lamellated structure.

Comment.—The difficulty in making a localizing diagnosis in this case was largely due to the fact that blindness precluded the employment of perimetry. From the situation of the tumor and its cystic projection into the calcarine region, it is most probable that hemianopsia was an early symptom. The case furnishes a good example of a decompression by widespread diastasis of the sutures which may take place in a child. The misleading cerebellar symptoms were apparently due to the downward dislocation of the left half of the tentorium with compression of

the pons and superior cerebellar peduncle. This is a matter which has been insufficiently emphasized in the literature. The case shows, furthermore, how a supratentorial lesion may produce internal hydrocephalus of high degree by compression of the iter.

At the present day, the lesion certainly would have been localized. If neurologic studies had not sufficed for this, the left ventricle would inevitably have been tapped in the course of the cerebellar operation, and almost certainly one of the cysts would have been entered. This procedure as a routine in cerebellar operations was not yet introduced. The case, moreover, represents one of the comparatively rare conditions in a blind patient with hydrocephalus when a ventriculogram in all proba-

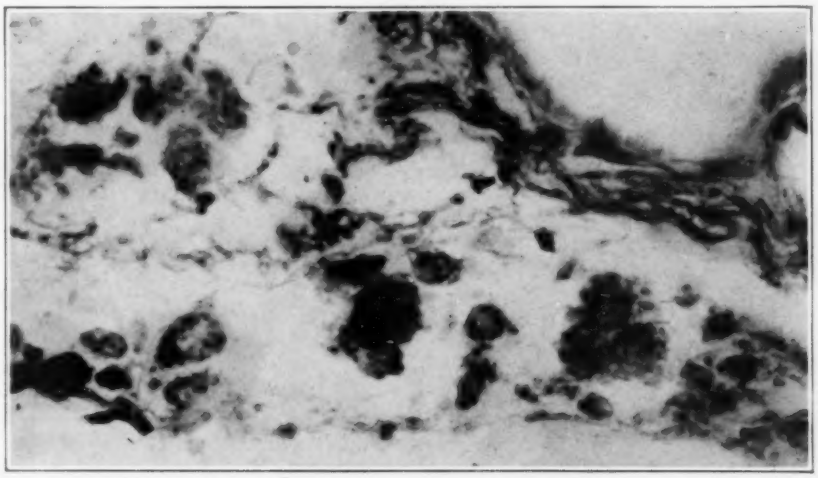


Fig. 11 (Case 2).—Definite granules in the protoplasm of the tumor cells (phosphotungstic acid-hematoxylin; × 850).

bility would today disclose an occipital lesion. Had the lesion been properly localized, in view of the surrounding cysts, it would have been most favorable for operative removal. As it was, the cerebellar exploration was probably the worst step that could have been taken, and the increase of symptoms was undoubtedly due to the further settling down against the already embarrassed pons and cerebellum of the supratentorial lesion.

CASE 3.—*Cystic papilloma of left lateral choroid plexus. Operation and early recurrence of symptoms after simple cyst evacuation. Death one year later.*

Feb. 9, 1915.—Admission of W. G. D., a man, aged 50, with the diagnosis of probable tumor.

Clinical History.—The patient, who had been a heavy drinker, contracted syphilis in 1893, was treated intensively for three years and was considered cured, although in 1896 he had iritis with cataract and loss of vision of the

left eye, and in 1900 a permanent left abducens palsy set in. He had no further neurologic symptoms till six months before admission, when he observed that writing was difficult, and soon he could not even sign his name. Then in reading he could not gather the meaning of the text. His speech became hesitant, and he often used the wrong word. One month later, he began having jacksonian attacks characterized by twitching of the muscles of the right side of the neck and subsequent spreading to the face and arm but without loss of consciousness. He subsequently had from eight to ten of these seizures. In November, 1914, his right arm became weak; soon his right foot began to drag in walking, and the right side of his face became paretic. Naturally,

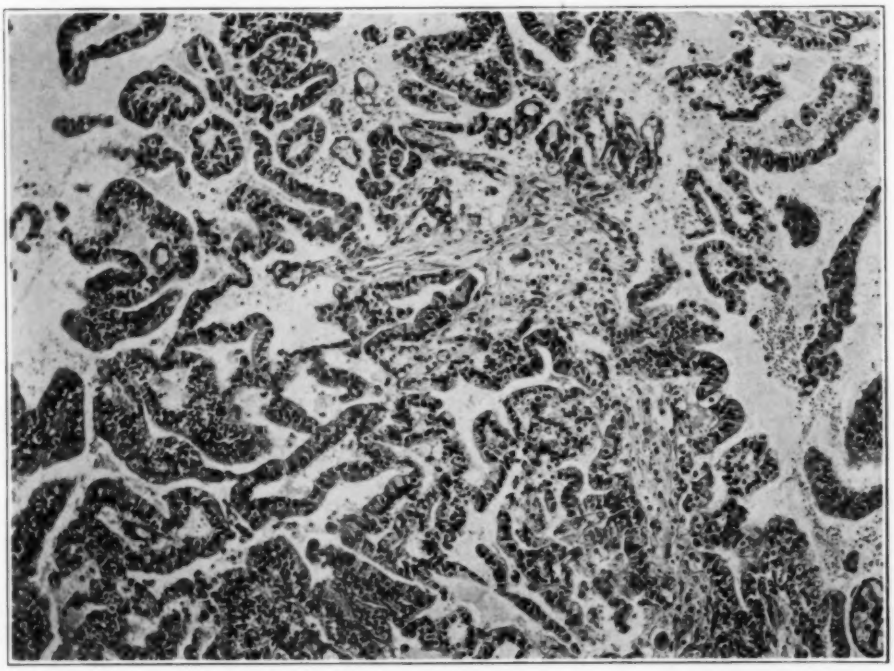


Fig. 12 (Case 3).—Papillomatous character of the cystic tumor which apparently arose from the left lateral choroid plexus. (Phosphotungstic acid-hematoxylin; × 80).

he had been treated with arsphenamin, although the blood and spinal fluid Wassermann reactions were negative. Some improvement in the hemiparesis had ensued.

Neurologic Findings.—The patient showed spastic hemiparesis chiefly involving the arm, but also the face and leg, with increased deep reflexes; no clonus, and normal plantar response; old iritis, with cataract of the left eye; left abducens paralysis. In addition, he showed some paraphasia, with slow and hesitating speech. There was no headache or choked disk.

Operation (Cushing).—On Feb. 17, 1915, a left osteoplastic flap was turned down, exposing a fairly tense cortex with flattened convolutions. Palpation revealed a cyst from which more than 100 c.c. of deep yellow fluid were

withdrawn by a puncture at the posterior end of the second frontal convolution. An incision was then made into the cyst, the walls of which were lined by a vascular brownish red growth, a section of which was removed for histologic study. Operative diagnosis: gliomatous cyst.

Clinical Course.—The patient made a good immediate postoperative recovery, with marked relief of all symptoms. Not long after his discharge, however, his jacksonian attacks recurred, and there was return of paralysis and aphasia. He refused to have the cyst tapped again, resorted to Christian Science, and died in July, only five months after operation. Necropsy was not performed.

Pathology.—Unfortunately for our present purposes, the fragment of the cyst wall removed for microscopic study was fixed in Zenker's solution. This fact has made it impossible to employ staining methods necessary for a detailed cytologic study.

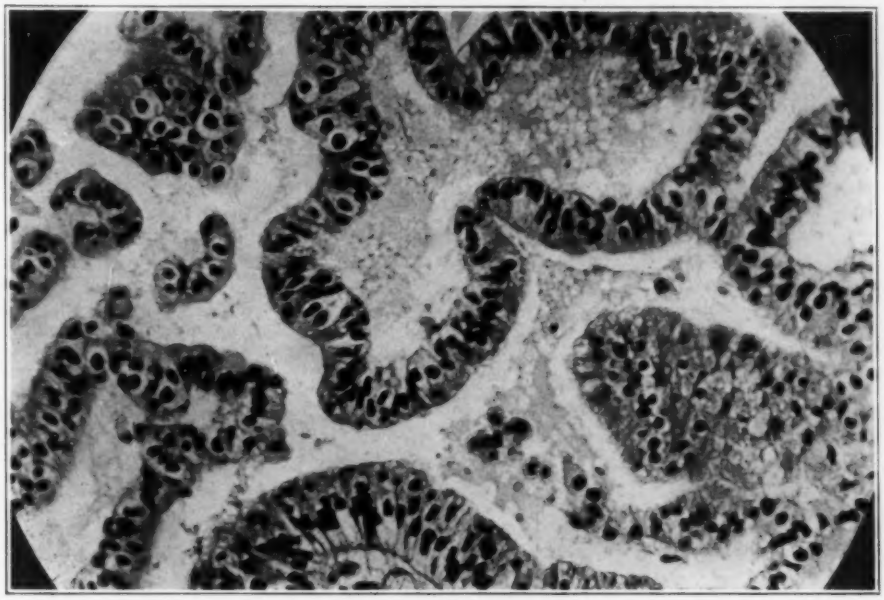


Fig. 13 (Case 3).—Character of the epithelium which varies from cuboidal to columnar; note the mucoid degeneration of the central core of the villi. (Zenker fixation; phosphotungstic acid-hematoxylin; × circa 300.)

The lesion proved to be a papillomatous growth (Figs. 12 and 13). The villi were long and narrow, and exhibited many side branches. Each of them contained a central core of fibrous connective tissue which had undergone more or less mucoid degeneration, but which showed nevertheless many thin-walled blood vessels. The villi were numerous and somewhat larger than those encountered in a normal choroid plexus. The epithelial cells in some places were cuboidal in shape, but in others, tall and columnar. The nuclei were centrally placed and varied from round to oval and cigar shapes. The cytoplasm was lightly stained and finely granular. Many of the cells in their apical portions showed clear areas which were regarded as vacuoles.

No corpora amylacae were observed. Everywhere the cell membrane was intact, and no mitotic figures were encountered. Blepharoplasten and glia fibers were absent.

Comment.—The localization of the lesion was more easily determined than its nature in this case. In spite of the negative Wassermann reactions, a syphiloma was the preferential diagnosis. This was changed in the operative note to a presumptive gliomatous cyst, owing to the highly colored and clotting xanthochromic fluid contents. The microscopic picture, however, definitely pointed to an origin from the lateral choroid plexus. The experience shows that one is not always justified in making a diagnosis of gliomatous cyst on the basis of a clotting straw-colored fluid from a tumor cavity. Had the true nature of the cyst been appreciated during the operation, a more radical exploration with wider transcortical incision would have been made. In all probability, there was a central ball of papilloma as in the preceding case, which might have been removed.

CASE 4.—*Suspected right parietal lesion. Exploration revealing hydrocephalus. Subsequent suboccipital operation disclosing a supposedly gliomatous cyst deep in right cerebellar hemisphere. Readmission with recurrence of symptoms. Verified papilloma of right cerebellar hemisphere. Death three months later.*

Aug. 6, 1919.—Admission of Winifred S., aged 30, with the complaint of periodic headaches, vomiting and numbness of left side.

Clinical History.—In March, 1919, the patient first complained of periodic attacks of numbness. These had a jacksonian "march" progressing from thumb to fingers to face, and came in attacks lasting about five minutes. She had had ten such seizures, none of them accompanied by loss of consciousness or motor symptoms. In July, she began having headaches. These would start in the suboccipital region and extend to the frontal areas. They were of brief duration, and were provoked by stooping. They were accompanied by vomiting and dizziness.

Neurologic Findings.—There was bilateral choked disk of 2 diopters. The right pupil was larger than the left. There was some incoordination of the left hand, and the muscle power was diminished on the left side. There was questionable left facial paresis. The tongue deviated to the left. The tendon reflexes were exaggerated on the left side. Though she gave a history of dizziness and staggering, no nystagmus or ataxia was disclosed. Station and gait were impossible to test because of dizziness.

Operation (Aug. 13, 1919). (Cushing).—Owing to a presumptive diagnosis of right postcentral tumor of the cerebrum, an osteoplastic flap was turned down. A tense brain was disclosed, with hydrocephalus but no local lesion. The flap was replaced after making a subtemporal decompression.

Clinical Course.—No relief was afforded by this operation. The choked disks became more pronounced and showed many hemorrhages. The subtemporal decompression remained full, and there was some elevation of the flap. A certain degree of hypotonicity and dysmetria became apparent on the left side. Even in the absence of nystagmus and other characteristic signs of a cerebellar lesion, the hydrocephalus was enough to make a subtentorial lesion probable.

Second Operation (Aug. 30, 1919).—A bilateral suboccipital exploration was carried out. The cerebellar hemispheres, though bulging, were normal in appearance and to palpation. A puncture of the lobe on the left (the suspected side) was negative. A puncture on the right entered a cyst at a depth of 5 cm. About 30 c.c. of yellow, rapidly clotting fluid were evacuated. Diagnosis: gliomatous cyst.

Clinical Course.—From this operation the patient made an excellent recovery, with practical abeyance of all symptoms. She was discharged on September 28, in excellent condition. Her period of relief was brief—more so than is usually the case after puncture of a gliomatous cyst. Two months after her discharge, the headaches returned. She became again increasingly unsteady, walked with a staggering gait, and would fall if not assisted. She began to

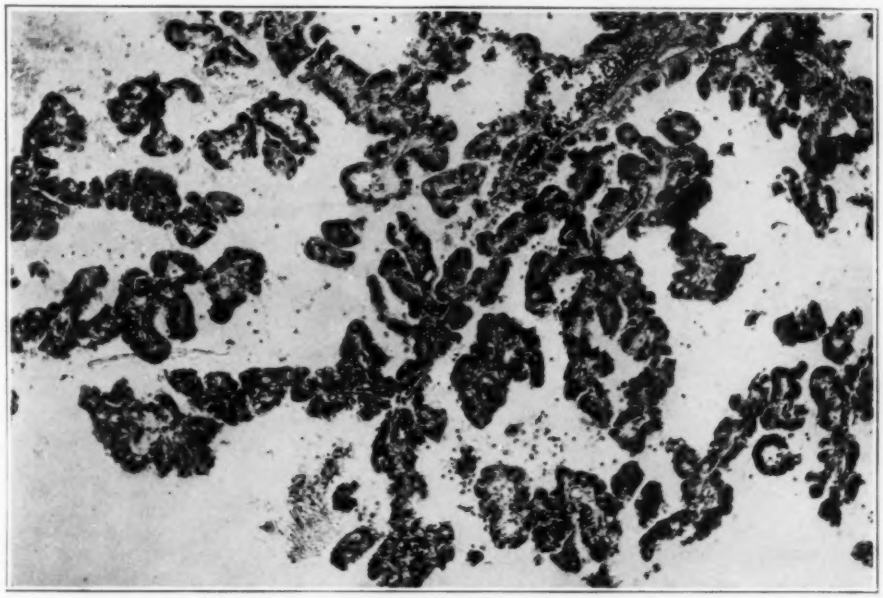


Fig. 14 (Case 4).—Typical villous-like arrangement of tumor. (Zenker fixation; hematoxylin-eosin stain; × 80.)

have difficulty in talking and swallowing. There was return of the same attacks of numbness on the left side of her face and tongue of which she had previously complained.

She reentered the hospital on Jan. 12, 1920. Examination showed bulging and tense subtemporal and subocipital areas of decompression. The optic disks were elevated 3 diopters. There was apparent for the first time coarse nystagmus to the right, marked incoordination of movements of the left side, staggering gait, dysarthria and dysphagia—in short, a full-blown right cerebellar syndrome. In the hope of avoiding further operation which offered little prospect of cure, an unsuccessful attempt was made, on one or two occasions, to puncture the cyst. She became progressively worse, and finally, after long hesitation and in spite of her poor condition, the cerebellum was reexplored.

Third Operation (March 13, 1920).—The old suboccipital wound was reopened, and the right hemisphere was found to be largely replaced by a soft, partly cystic tumor, which from its gross appearance was mistaken for a cystic glioma. Some of the tissue was scooped out for examination, but the lesion was more vascular than the usual glioma, and a radical extirpation was not undertaken.

Clinical Course.—She made a surprisingly good recovery from this operation, though her local symptoms were not greatly altered. She was discharged on April 12. Her death was reported as having occurred on July 24. Necropsy was not performed.

Pathology.—The portion of tumor removed for microscopic study was fixed in Zenker's fluid. The pathologic report at the time was a "papillary carcinoma of the choroid plexus." Reexamination of the tissues showed numerous villi which were somewhat larger than normal and much more numerous (Fig. 14). They had a characteristic cauliflower-like appearance. The central core of each villus consisted of loose white fibrous connective tissue containing numerous blood vessels. The epithelial cells covering these villi were cuboidal in shape, and were arranged in a single layer. The nuclei were round and placed centrally. Many vacuoles were present in the cytoplasm of these cells and for the most part in the apical portion. The cytoplasm was finely granular and stained lightly. No corpora amylacae were found. Owing to the nature of fixation of the tissue, a more detailed study of the cytology is precluded.

Comment.—In this case, we were at first entirely misled by the supposedly cortical origin of the sensory attacks of numbness which were thought to have jacksonian characteristics. Such signs in the absence of a definite cerebellar syndrome are often misleading. They were probably due to pressure on the sensory tracts within the medulla. Too little emphasis was laid on the history of unsteadiness. Because of inability to assume an erect posture without dizziness and vomiting, the patient's station was not observed.

Not until the hydrocephalus had been disclosed was the presence of a subtentorial lesion seriously considered. Even so the lesion was wrongly lateralized and found on the right rather than on the left side. In view of the absence of nystagmus, a median rather than a lateral lesion might have been expected. The tumor, as in Case 1, doubtless originated from the lateral plexus in the region of the foramen of Luschka. In the absence of clinical signs pointing to the cerebellopontiie angle, the recess was not investigated at the first operation. The tumor apparently had invasive characteristics, and may represent the type of papilloma often termed carcinomatous.

The two following cases were much more favorable from a surgical standpoint than those heretofore recorded.

CASE 5.—*Disclosure at operation of a papilloma of the fourth ventricle projecting into spinal canal. Fragmentary removal for verification. Recovery.*

March 5, 1923.—Admission of Mrs. Edith H. S., aged 27. Because of enlargement of the sella, she was supposed to have a pituitary tumor.

Clinical History.—For eighteen months, she had noted failure of vision with unsteady gait and some incoordination of the lower extremities. For most of her life, she had suffered from frontal headaches. These frontal headaches had become more severe during the past year and were now associated with dizziness. She began to have marked diminution of vision ten weeks before entering the hospital, and for three weeks the right eye had been blind. There had been frequent periods of amblyopia. She was conscious of movement of objects from left to right in front of her. She ascribed her unsteadiness to visual disability .

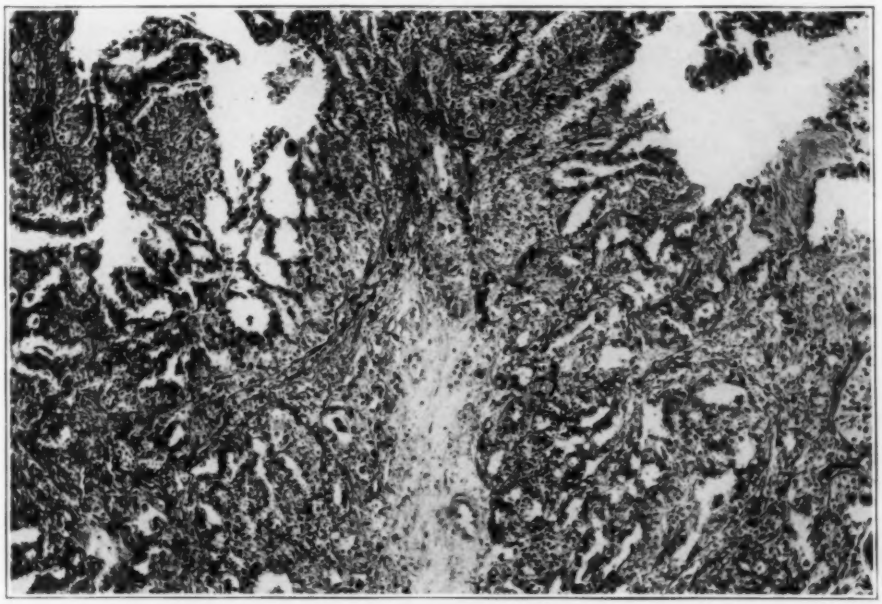


Fig. 15 (Case 5).—Papillomatous nature of the tumor under low power magnification. (Zenker fixation; phosphotungstic acid-hematoxylin; × 80.)

Neurologic Findings.—There was bilateral choked disk of 4 to 5 diopters, with advanced secondary atrophy, the process being more advanced on the left. The pupils were dilated: reaction to light and accommodation was poor. Sustained and coarse nystagmus was induced by looking to either side, but particularly to the left. The Romberg sign was positive, with retropulsion. Incoordination was marked, especially of the lower extremities. She walked with a wide base and turned with difficulty. She was unable to stand alone on either foot. Diagnosis: a cerebellar, possibly a midline, tumor.

Operation (March 10, 1923). (Horrax).—Usual suboccipital exposure after ventricular tap disclosed hydrocephalus. A round, grayish tumor, the size of a nutmeg on its exposed portion, was found lying low down between the cerebellar hemispheres. It extended downward through the foramen magnum, necessitating for its full surface exposure the removal of the posterior arch of the atlas. The growth was highly vascularized and was surrounded on all

sides and over the surface by pulsating arteries. It was thought unwise to attempt extirpation, but a fragment was removed for histologic study. The presumptive diagnosis at the operating table was ependymoma of the fourth ventricle.

Postoperative Course.—The patient made an excellent recovery. The choked disk completely subsided in the right eye, but at the time of her discharge, on April 7, there was still 2 diopters' elevation of the left nerve head, with retention of good reading vision despite marked secondary atrophy. She received one roentgen-ray treatment before leaving the hospital. Soon after she returned to her home in England. A report by letter, Sept. 25, 1924, eighteen months from the time of her operation, stated that she remains in good condition with a minimum of discomfort and some vision preserved in her left eye.

Pathology.—The fragment of tumor removed was fixed in Zenker's fluid and was therefore unfit for many cytologic methods. Microscopically, the tissue had the characteristic papillomatous structure which identified it as having originated from the choroid plexus. The villi were numerous, long, wide and possessed many side branches. The central core consisted of a dense, white, fibrous connective tissue with blood vessels. The epithelial cells were cuboidal in shape, and the cytoplasm was finely granular. The nuclei were round, stained darkly and for the most part were placed centrally. The tissue was highly vascular. The blood vessels had very thin walls and resembled blood sinuses (Fig. 15).

There could be no doubt of the localizing diagnosis of this case, at least in placing the lesion below the tentorium. A distension of the sella resulting from dilatation of the third ventricle is, or should be, well known as a common accompaniment of posterior lesions producing hydrocephalus. The tumor which was disclosed might well enough have been regarded as an unverified ependymoma. Whether the lesion will retain its purely papillary characteristics and be damaging only from its size as in Case 1, time only can tell. The suboccipital decompression so far as known has relieved the patient of her discomforts, and, fortunately, has preserved some vision.

CASE 6.—*Suspected acoustic neuroma. Suboccipital exploration. Extirpation of midline tumor of the choroid plexus of the fourth ventricle. Recovery.*

June 19, 1923.—Admission of Robert W. H., aged 28.

Clinical History.—The past history was uneventful except for a cranial trauma received during childhood, which produced unconsciousness for several hours. This left no trace. The patient had always enjoyed good health and vigor, but when examined for military service in 1918, he was found to have unsuspected relative deafness in his left ear.

In March, 1923, he began to have occipital headaches. These headaches came in three severe attacks in as many weeks, with vomiting, a sense of fulness and discomfort in the suboccipital region, and on one occasion with stupor for several days. At the same time, unsteadiness of gait was first observed, and this was always accentuated during an attack of headache. He gave a history of subjective diplopia with his bad attacks and also of subjective numbness of the right side of the face.

Neurologic Findings.—There was a bilateral choked disk of 2 diopters. Coarse and well sustained nystagmus on looking to the right was present. There was a suggestive Romberg sign with a tendency to fall to the right. The gait was fairly steady, but turning quickly brought unsteadiness. There was definite asynergy in the right lower extremity. There were suboccipital tenderness and rigidity. Auditory acuity was diminished on the right, and the right cornea was less sensitive. Presumptive diagnosis: right acoustic neurinoma.

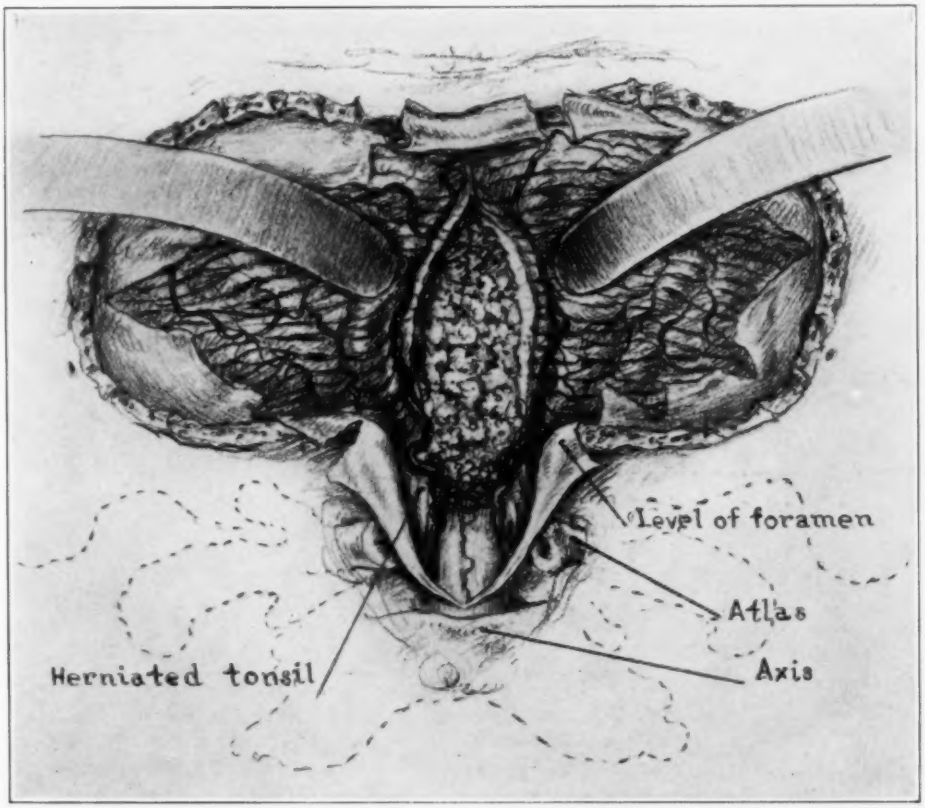


Fig. 16 (Case 6).—Appearance of the tumor as exposed after removal of the arch of the atlas and vertical incision of the vermus. Actually the growth was a roundish mass, here only partially exposed.

Operation (June 26, 1923). (Cushing).—The customary bilateral exploration was made with puncture of the ventricle, disclosing hydrocephalus. A large, thick, grayish arachnoid membrane was exposed and not immediately opened. Exploration of the lateral recesses revealed no lesion. On then opening the posterior cistern, marked herniation of the cerebellar tonsils into the spinal canal was disclosed. On drawing up and separating the tonsils, the nubbin of a papillary tumor was seen projecting down into the foramen magnum. To bring the growth into view, it was necessary to remove the posterior arch

of the atlas and finally to split the vermis cerebelli the full extent of the exposed field (Fig. 16). Two large sized arteries passed up on each side of the tumor, and there was a communicating branch just below it. The growth was sufficiently firm to be handled without tearing. It was eventually dislodged after prolonged manipulations, without injury to any vessels which could not be previously "clipped." The exposed floor of the fourth ventricle was widely distended and depressed. One could look into the greatly dilated iter from which fluid poured.

Postoperative Course.—For some days, he showed the irregular pyrexia not uncommon after extensive cerebellar operations. The bloody cerebrospinal fluid drawn off by lumbar puncture on two occasions was sterile. He improved rapidly. The papilledema soon subsided. Some nystagmus and slight incoordination of the upper extremities and staggering gait were still present on July 20, 1923, the time of his discharge.

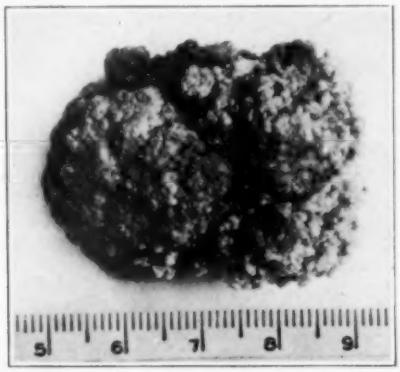


Fig. 17 (Case 6).—Papillary appearance of the tumor as removed.

End-Result (June 26, 1924).—The patient wrote a year to the day after the operation that he was in perfect health and had no residual symptoms.

Pathology.—The ball of tumor about 4.5 cm. in diameter weighed 28 gm. It had a tufted and wartlike surface. It had apparently been removed intact (Fig. 17). Fragments were immediately fixed both in Zenker's and formalin solutions. Microscopic sections revealed the typical papillomatous appearance (Fig. 18), with villi much larger than those encountered in a normal choroid plexus. The central core contained very little white fibrous tissue, being made up for the most part of a loose reticular tissue. There were numerous blood vessels with very thin walls. The epithelial cells were tall and columnar with oval or cylindrical centrally placed nuclei. The cells were two or three layers deep in some areas (Fig. 18), while in others they were arranged in a single layer, and many of them contained clear round or globular areas. Very fine, darkly stained granules were present in the basilar portion of the cytoplasm. These granules appeared to be similar, and showed the same staining characteristics as those found in the cells of normal plexuses. They were, however, much less numerous and much smaller in size.

Comment.—This, the last and most favorable case in the series, represents an unusual experience. With the exception of the case of

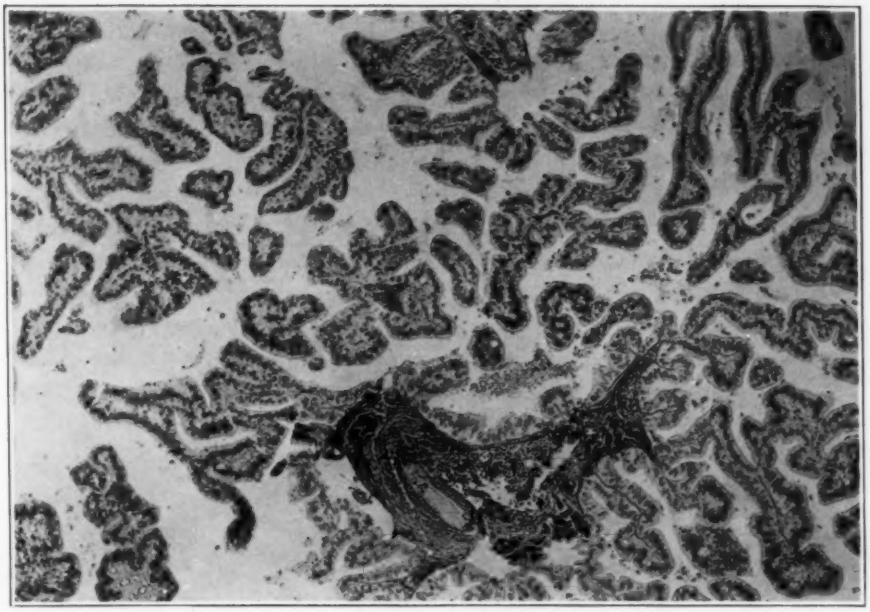


Fig. 18 (Case 6).—Villous-like arrangement of cells, with central core of connective tissue. (Mallory's connective tissue stain; × 80.)

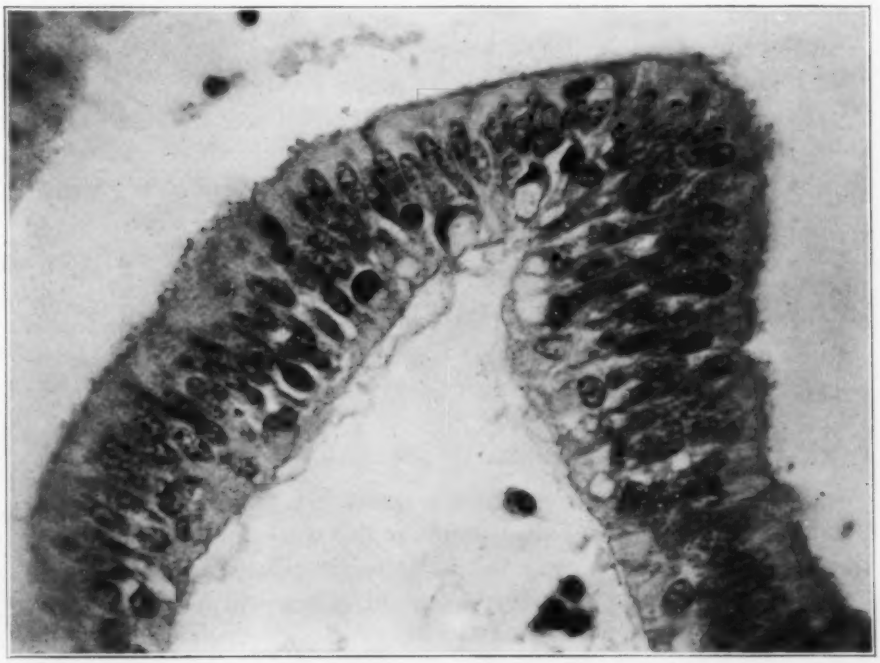


Fig. 19 (Case 6).—Many layered columnar epithelium clothing the villi. (Phosphotungstic acid-hematoxylin; × 850.)

very similar nature reported by Dr. Sachs, it appears to be the only example in the literature of a successful extirpation of one of these rare papillary tumors arising from the tela choroidea of the fourth ventricle. An incorrect localizing diagnosis had been made owing to a misinterpretation of symptoms suggesting a lesion in the right cerebellopontile angle. After the nerves in the recess had been exposed without finding a lesion, the operator was about to close the wound, believing that the case was merely one of cisternal arachnoiditis.[22] The lesson to be drawn from this is that in a cerebellar exploration for tumor close scrutiny should always be given to the low median field whenever there is marked and bilaterally symmetrical cerebellar herniation through the foramen magnum.

These midline cerebellar tumors are often spoken of as tumors of the fourth ventricle. Because of their seat of origin, they inevitably deform and distend the ventricle, and often crowd their way downward into the spinal canal. It is not an uncommon seat of origin for tumors, as shown by the material at our command for study. Most of the cases in the series are spongioblastomas (neuroblastomas)—twenty-eight cases. Next in order are the ependymomas (eight cases), and still more rare than the papillomas are the epidermoid or dermoid cholesteatomas of this region (three cases). These lesions of course cannot come from the same anlage, but the structures around the roof of the fourth ventricle have a complicated development, and it is perhaps not unnatural that this should be a frequent seat of tumor formation.

Experience should make it possible to distinguish these several lesions from their naked eye appearance at the time of operation, but whether we may ever reach a point of making more than a guess as to their character at the bedside before operation is unlikely. In view of the greater frequency of the spongioblastomas in this neighborhood, particularly in the case of children who show hydrocephalus with a marked cerebellar syndrome in which nystagmus is wanting, this naturally would be a preferential diagnosis on the grounds of probability, and it has been correctly made in several of the twenty-eight cases.

GENERAL DISCUSSION

It should be the ambition of the neurosurgeon to be able not only to localize a tumor with sufficient accuracy to expose it in the way most favorable for operative removal, but also, if possible, to foretell its pathologic nature, for on this the line of attack will largely depend. This ambition can now be realized with a fair percentage of success in

22. Horrax, G.: Generalized Cisternal Arachnoiditis Simulating Cerebellar Tumor, Arch. Surg. **9**:95-112, 1924.

most of the tumors in and about the region of the chiasm and hypophysis, in the majority of the tumors in the cerebellopontile angle, in a large number of the meningiomas of various situations and, as stated above, in a few of the midcerebellar spongioblastomas of childhood.

When tumors, however, are so rarely encountered as those of the choroid plexus, one's clinical experience is too slender to form a reliable basis for any such well-rounded preoperative diagnosis. The histories which have been given of these six papillomas observed over a period of fifteen years, show not only how imperfect in the past have been the localizing diagnoses, but how difficult it has been, except possibly in Case 1 and Case 6, for the surgeon to tell even when the lesion was exposed that he was dealing with a benign plexus tumor.

We are not justified, therefore, in drawing too many conclusions from this small experience, and from a surgical standpoint the literature is as silent as from a pathologic standpoint it is confusing. Attention, however, may be called to a few considerations. Four of the tumors were subtentorial, the growths being median and arising almost certainly from the tela choroidea in two instances (Cases 5 and 6), and from the lateral cerebellar recess in two others (Cases 1 and 4). On the other hand, two of the tumors arose from the plexus of the lateral cerebral ventricles. One striking characteristic of the latter tumors was their association with enveloping cysts, which indeed may have been true of the tumor in Case 4. In one instance, the major cyst projected toward the occipital lobe. In the other, it presented in the left midhemisphere. Whether all of these lesions at any early stage were precisely similar in their gross characteristics and consisted of a simple papillomatous mass such as was encountered in Case 6 can only be surmised. In all probability, they have so originated, but, owing to the fact that the cells of the tumor had "secretory activity," cystic spaces were thus formed after the growth had reached a sufficient size to become imprisoned in the nervous tissue. It is assumed, in short, that the tumor cells elaborate fluid just as do those of the normal plexus. This fluid in the early stages of the growth simply empties into the ventricular cavities or subarachnoid cisternae. When, however, the growth finally becomes sufficiently enveloped by the deformed nervous tissues, the secretion becomes pocketed with resultant cyst formation.

Microscopically, all of the tumors showed villi with a central core of connective tissue and were covered by typical plexus cells which for the most part were cuboidal in shape and arranged in single layers like those of a normal plexus. In cases in which the tissues had been properly fixed for the purpose, round granules, generally situated about the nucleus, could be easily demonstrated in the protoplasm of the cells—granules which are shown by the usual strains for mitochondria. On

the other hand, they do not stain by ethyl violet-orange G, a reagent by which the common secretory granules, found for example in the pancreas, may be identified. It may be assumed therefore that these granules are of the nature of mitochondria. "Blepharoplasten" and glia fibers were not found in any of the sections, and their absence of course makes possible the differentiation of such tumors as we have here considered from ependymomas and the rare ventricular papillomas of subependymal origin.

When one considers how meager and obscure is the pathologic description of these plexus papillomas, there can be no occasion for surprise that the surgical aspects of the subject have hardly been touched on. However, in consideration of the number of intracranial explorations which are today being made in many surgical centers, these tumors in spite of their rarity must certainly be brought into view occasionally. They are likely to be neglected unless neurosurgeons come to recognize them at operation and to realize that the papillary variety is surgically removable. In short, a lesion which has formerly been a pathologic curiosity becomes a matter of definite surgical importance.

SUMMARY

1. Some twenty examples of true papilloma of the choroid plexus are to be identified in the literature. They are to be found scattered under most varied titles and are generally confused with tumors of other sorts which project into the ventricles. In a series of 964 verified intracranial tumors, six of these papillomas have been encountered. Two arose from the lateral choroid plexus and four from the plexus of the fourth ventricle. In five cases, the lesion was identified by tissues removed at operation; in one, at necropsy.

2. In three of the tumors, an accompanying cystic formation was a striking characteristic. In the other three, the tumor was a simple cauliflower-like papilloma. In all cases, however, the sections show villi with a central well vascularized core of connective tissue covered by cuboidal epithelium, usually in a single layer.

3. The epithelial cells of these papillomas contain round, darkly staining granules, which tend to be arranged perinuclearly, and which appear to be closely related to mitochondria. The tumors do not contain glia fibers, nor do their cells show "blepharoplasten." They are therefore not to be confused with the papillomatous ependymomas.

POSITION OF THE HEAD IN CEREBRAL TUMORS ABOVE AND BELOW THE TENTORIUM *

H. W. STENVERS, M.D.

UTRECHT, HOLLAND

The position of the head in cases of cerebral tumor is sometimes a phenomenon of sufficient importance to deserve careful analysis.

At present, I shall consider only those positions which appear to be forced and which the patient assumes because he cannot do otherwise even if he should wish to, or because this position is the most agreeable to him. I shall not consider the faulty position of the head due to diplopia, etc.

In the majority of cases, the position of the head is to be considered as the result of some defective postural reaction of a general nature. For instance, a certain patient with a tumor of the frontal lobe lies in bed with his head straight. If, however, he attempts to walk (in which case he walks backward and mostly toward the unaffected side), his head assumes a typical position, that is, bent toward the healthy side and somewhat turned toward the diseased side.

DISCUSSION OF LITERATURE

Remarkably little is found in the literature concerning pathologic positions of the head.

In 1898, Oppenheim pointed out the great importance of the position of the head in cases of cerebral tumors, without, however, explaining the probable mechanism through which it is assumed.

In 1903, F. E. Batten [1] gave an excellent clinical description of some typical cases of cerebellar tumor and came to the following conclusions:

1. Diseases of the cerebellum often produce a characteristic attitude of the head. The ear inclines to the shoulder on the unaffected side and the face turns toward the diseased side.

2. The inclination of the head is contrary to that found in experimental injury to the cerebellum, and the rotation of the head is in accordance with the experimental results.

3. Not too much reliance must be placed on the position of the head since similar displacements also occur in cases in which there is no gross lesion of the cerebellum.

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* From the Neuropsychiatric Clinic of the University of Utrecht; Director, Prof. Cornelius Winkler.

1. Batten: On the Diagnostic Value of the Position of the Head in Cases of Cerebellar Disease, Brain **31**:72, 1903.

Batten attempts to account for the position of the head by assuming the presence of a particular center for this function in the central nervous system.

Hulshoff Pol,[2] in 1905, described the position of the head in a case of ventricular tumor and also looked for the solution of the problem in the central nervous system. Totally under the influence of Bolk's theory of localization in the cerebellum, he drew up the hypothesis that the position was provoked by pressure of the tumor on the lobus simplex.

This explanation is not satisfactory, because, as Batten had noted, the position may occur without any lesion of the lobus simplex.

In 1908, Gordon [3] noted in a series of cases only partly verified by necropsy that peculiar varying positions of the head are assumed, but he did not venture to explain the reason for them.

Laruelle,[4] like Batten, described the position of the head in a patient with a right-sided cerebellar tumor, but he also gave us no further explanation of the cause of this position.

In 1921, Kluge [5] described a patient with a cyst in the left hemisphere of the cerebellum. This patient held his head rigidly bent forward fixing his eyes on the ground. Sudden death resulted when he bent his head backward.

Mingazzini, in his monograph on the corpus collosum, described the opposite position of the head. On page 107, he speaks about a patient with a tumor of the corpus callosum, who had a violent headache: "Vom im Bette liegenden Patiente wird der Kopf nach hinten gebeugt."

Mingazzini does not give an explanation of this position of the head. Nowhere do we find these positions of the head discussed as a separate topic.

ANATOMY AND PHYSIOLOGY OF THE MOVEMENTS OF THE HEAD

Since we are discussing here disturbances in the posture of the head, it will be necessary first to explain what physiologic and mechanical factors enter into this complex function.

In movements of the head (and I confine myself here chiefly to forward and backward bending), we can distinguish several anatomic relationships which are of particular importance:

1. The atlanto-occipital articulation.

2. The relationship of the clivus to the posterior rim of the foramen magnum.

2. Pol, Hulshoff: Een tumor in den vierden ventrikel met druk op den lobus simplex, Psychiat. e. Neurol. Bl **9**:505, 1905.

3. Gordon, A.: A Special Diagnostic Phenomenon in Cerebellar Diseases, J. A. M. A. **51**:461 (Aug. 8) 1908.

4. Laruelle: Rev. neurol. 1906, no. 4, p. 204.

5. Kluge, A.: Ztschr. f. d. ges Neurol. u. Psychiat. **73**:606, 1921.

3. The relationship of the dura to the skull and vertebrae.

4. The relationship of the medulla oblongata to the cisternae.

5. The mutual relationship of the cerebral ventricles.

6. The relationship to one another of the membranes in the skull (tentorium and falx cerebri).

1. The mechanics of the atlanto-occipital articulation are generally treated extremely lightly in the textbooks. R. Fick [6] gives a careful description of this joint. He points out, in the first place, that with all movements of the head more or less considerable movements of the neck also occur.

The movements which take place at the atlanto-occipital joint are, first, nodding, and then lateral inclination of the head, which is always combined with rotation to the opposite side.

This double movement occurs because the articular surface has a curve in the anteroposterior as well as in the lateral direction.

The axis of curvature for the anteroposterior movement is different in its anterior and in its posterior portions. The axis usually runs through a point just above the lateral edge of the occipital condyles, whereas the axis of curvature for lateral inclination runs through the middle of the clivus.

From the central position, the joint is movable about 20 degrees in the forward direction and 30 degrees in the backward direction. The lateral inclination amounts to from 15 to 20 degrees.

I wish to lay particular stress on the great similarity of the positions described by Batten in cases of cerebellar disease, and the possibility of such movements in the atlanto-occipital joint. This is not accidental.

2. During movement in the atlanto-occipital joint, a complete change takes place in the shape of the bony frame surrounding the base of the brain. We may easily convince ourselves of this on the cadaver after removal of the brain.

When the head is bent forward, the clivus slides, as it were, over the dentate process of the axis, and forms a rather acute angle with it. The posterior edge of the foramen magnum at the same time moves upward and backward. It is astonishing to see how when the head is bent forward, the dentate process becomes visible through the foramen magnum.

When the head is bent backward, the appearance is different. Then the clivus is depressed to the level of the dentate process, and the angle is obliterated. The posterior edge of the foramen magnum moves downward and forward.

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6. Fick: Handbuch der Anatomie und Mechanik der Gelenke, 1910.

3. When the head is bent forward, the dura is stretched both anteriorly and posteriorly; when it is bent backward, the dura is relaxed.

4. The medulla oblongata is located just at the junction between the skull and the vertebral column, but during movements at the atlanto-occipital articulation, it is effectually protected by large spaces filled with fluid which surround it. The cisterna cerebellomedullaris (cisterna magna) is the largest of these. The fourth ventricle discharges its fluid into these cysts through the foramina of Magendie and Luschka.

5. The relationship of the cerebral ventricles to one another, more especially the third and fourth ventricles, is considerably altered by the various positions of the head. The fourth ventricle, which lies close to the axis of rotation of the skull in the anteroposterior direction, is only slightly displaced, whereas the third ventricle undergoes a great displacement. The consequence of this is that in the forward position the connecting channel (aqueduct of Sylvius) is curved, whereas in the backward position, the angle in the connecting channel has disappeared, and the third and fourth ventricles lie on the same level.

6. The relations of the membranes in the skull do not change during movements of the head. Pressure in the cranial cavity caused by processes above the tentorium will be most critical at the spot of least resistance, that is, at the point where the brain stem passes through the tentorium.

These are the principal factors which must be considered alone and in conjunction in order to explain the positions of the head in cases of intracranial tumor.

CLINICAL CASES

Case 1.—The first case which drew my attention particularly to this question of the position of the head, occurred in a boy, aged 18 years, who since his fifteenth year had complained of headache and giddiness. In May, 1920, he was admitted to the "Psychiatrisch-Neurologische Kliniek" at Utrecht.

The headache was on the right side of the forehead and in the neck. On the morning before his admission, he could not straighten his head, which was then bent strongly backward. Recently his gait had been unsteady.

The boy had marked papillitis with beginning optic atrophy. His head was markedly bent backward. The house physician on seeing the prominent upper cervical vertebra thought of the possibility of a vertebral luxation, and he immediately applied a Glisson apparatus. I state this here on purpose, since it is a good demonstration of the impression made by such a posture.

A positive clinical diagnosis could not be made.

Necropsy disclosed a large cystic tumor in the right occipital pole (Fig. 1).

In this case, a forced position of the head, maximally backward, was caused by a tumor above the tentorium.

Case 2.—The second case occurred in a patient with a glioma of the cerebrum. He was subjected to a palliative decompression, and is still living. The patient stated that when he had a violent headache he obtained relief

by bending his head far backward. The accompanying photograph shows this posture distinctly (Fig. 2).

Case 3.—The third case is a classical instance of the position of the head in cases of tumors of the posterior fossa.

On admission, the young man's head was bent far forward, inclined slightly to the right and rotated somewhat to the left (Fig. 3).

By means of other clinical data, which I omit, the diagnosis of a tumor of the cerebellum in the midline was made. At operation, the posterior rim

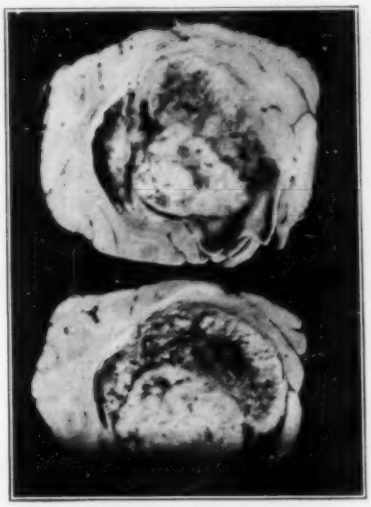

Fig. 1 (Case 1).—Large cystic tumor of occipital pole. Patient's head was bent far backward.

Fig. 2 (Case 2).—Unverified glioma of the cerebrum. The patient obtained relief from violent headache by assuming this position.

of the foramen magnum and the thinner portions of the occipital bone were removed. The dura was not opened, but a needle thrust toward the midline encountered a cyst containing clear amber fluid.

After operation the position of the head returned to normal, and there was not the slightest tendency to assume a forced position (Fig. 4).

The gait gradually became more impaired some months later, but no forced position of the head was observed. Operation was again performed, and this time the dura was opened. The patient did not recover.

Necropsy showed how the relationships in the posterior fossa had been disturbed. On longitudinal section, the anterior part of the ventricle was dilated and the posterior part entirely filled by the tumor. Evidently, by blocking the foramina of Magendi and Luschka, the tumor had caused a great increase in pressure, with consequent dilation.

Case 4.—The fourth patient (Fig. 5) also showed a marked forward inclination of the head, especially during paroxysms of headache.

Fig. 3 (Case 3).—Tumor of the cerebellum (Fig. 4). The forward position of the head was forced.

Fig. 4 (Case 3).—Cerebellar tumor after palliative operation. The patient carried his head in a normal manner.

At necropsy, a tubercle of rather large dimensions was found on either side of the median line in the inferior lobes of the cerebellum.

Case 5.—Recently I saw a boy with a strongly forced posture in the forward direction. There was some inclination to the right and slight rotation to the left.

Although he had never complained of a pain in the back of his head, and notwithstanding the fact that there was anosmia on the left side, on the grounds of this position of the head, I was compelled to diagnose a tumor in the posterior cranial fossa. An operative intervention was proposed, but was refused.

A month later, the pains became so unbearable that the patient insisted on an operative intervention. Then for the first time it was stated that pains in the neck also occurred.

At the operation, a large tumor was found in the left hemisphere of the cerebellum extending posteriorly and toward the midline. On opening the cisterna cerebellomedullaris, a small quantity of fluid escaped under very high pressure; but afterward no more came. When the probe was introduced in a caudal direction, fluid came profusely; but probing upward allowed no more fluid to escape.

Here, therefore, there was a free communication between the cisterna cerebellomedullaris and the spinal canal, but not between the cisterna and the fourth ventricle.

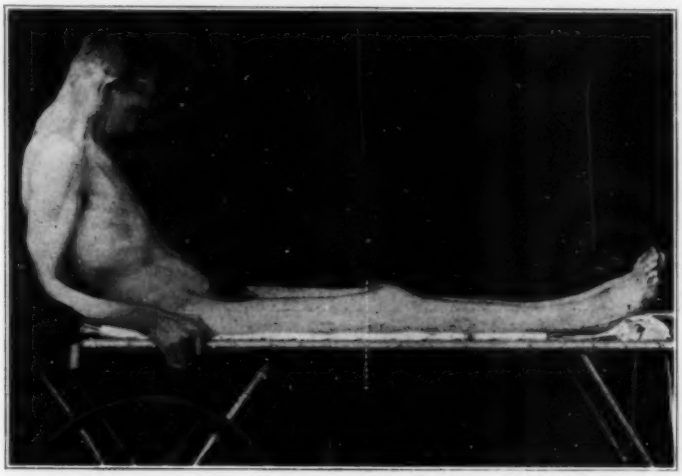

Fig. 5 (Case 4).—Tuberculoma of the cerebellum causing forced forward position of the head.

CASE 6.—The sixth patient, the one that I described in my thesis in 1920,[7] did not show any forced posture (Fig. 6).

In her case, a ventricular tumor was found. It was surrounded on all sides by cerebellar tissue, was embedded in it, and had no tendency to expand outward toward the cisterna. In this case, the fourth ventricle was almost entirely obliterated, and elevating the cerebellum would tend to make matters worse rather than better with regard to the closure of the ventricle.

CASE 7.—In this case, which presented many diagnostic difficulties, there was not the slightest tendency to a forced position of the head. The patient had a papillomatous tumor that filled the whole ventricular cavity in the posterior part, but which on account of its soft consistency, adapted itself completely to the shape of the cavity (Fig. 7).

This patient only mentioned that bending the head quickly backward caused giddiness and a painful spasm of the gastric musculature which persisted about a minute.

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7. Stenvers, H. W.: Klinische studie over de functie van het cerebellum en de diagnostick der cerebellum en bruggehoektumoren, Utrecht, 1920, p. 102.

Fig. 6 (Case 6).—Intracerebellar tumor that caused no forced position of the head.

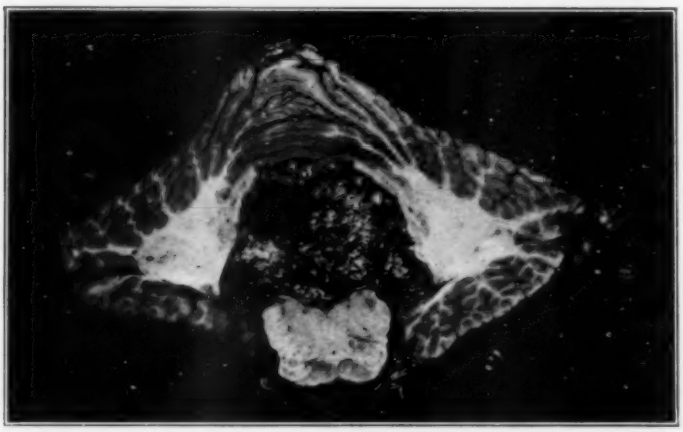

Fig. 7 (Case 7).—Soft papillomatous tumor in the fourth ventricle causing no forced position of the head.

Case 8.—This patient at first showed no forced position of the head. Early in the course of the disease, he had noticed that if he bent his head backward when lying down he could see nothing for a moment, and became giddy, whereas some moments later he was all right again. Two years later, he even stated that he was much troubled by paroxysms of pain in his neck, during which his head was retracted. Figure 8 shows the appearance of the fourth ventricle and the tumor in this case.

Case 9.—The ninth case is remarkable because the position of the head lead to the right diagnosis.

Fig. 8 (Case 8).—Tumor projecting into the fourth ventricle. The patient had attacks of retraction of the head.

The boy became ill, with all the symptoms of cerebellar tumor. He had violent headaches, and time and again his breathing stopped. Although cerebellar tumor was diagnosed with considerable certainty, the retracted position of the head gave rise to the suspicion that there might be a meningeal complication. A tubercle with meningeal dissemination was suspected; the boy, however, never had any rise of temperature. On account of the respiratory embarrassment, no occipital intervention was undertaken, and a subtemporal decompression was performed to lessen the headache.

Necropsy showed that there was a tumor in the cerebellum, but in addition a rather rare infiltration of the pia, which proved to be of a malignant nature.

Case 10.—Figure 9 shows a rapidly growing glioma of the left brachium pontis and left cerebellum in a patient who showed no forced position of the head.

COMMENT

What conclusions may be drawn from the foregoing cases?

I have confined myself to observations verified by necropsy (eight cases) or by operation (two cases).

1. The tumors (Cases 1 and 2) above the tentorium sometimes cause a forced position of the head backward.

2. Tumors of the posterior cranial fossa may cause a forced position forward. They appear to do so if by means of this forced position the communication of the fourth ventricle with the cisterna cerebello-

Fig. 9 (Case 10).—Glioma of the brachium pontis in a case with no forced position of the head.

medullaris is opened. If the blocking is such that movement of the cerebellum causes no change, then the forced position fails to appear.

Therefore we are most apt to find the forced position: (*a*) with tumors which lie in the midline and in the most distal portion of the cerebellum; (*b*) with tumors in the fourth ventricle which extend parallel to the medulla or penetrate between cerebellum and medulla without fusing with the cerebellum.

3. Meningeal complications alter the position of the head.

The explanation of these positions of the head is obvious if we take into consideration the physiologic basis that was discussed at the beginning of this paper. It is therefore improbable that they are caused by disturbances of innervation resulting from lesions of the cerebellum or elsewhere.

We agree with Batten that the position appears in cases of large tumors of the cerebellum as well as in those which produce hardly any change in that organ.

In the second place, we can say that the position of the head is dependent on the motor possibilities which Fick described in the atlanto-occipital joint.

In the third place, it is probable that the cause of the forced postures is mechanical rather than nervous, based on the fact that removing of the posterior rim of the foramen magnum causes the abnormal position to disappear, even if the disease progresses in the cerebellum or elsewhere.

Fig. 10 (Case 11).—Retraction of head in a case of subtentorial growth.

It is extremely difficult to explain the retracted position of the head by disturbances of innervation in cases of tumors above the tentorium.

How is this position brought about?

If there is a tumor in the cranial cavity above the tentorium, the rise of the pressure caused by this tumor will produce its most marked effects at the point of least resistance, that is, at the opening in the tentorium which is left for the penetration of the brain stem.

When the head is bent forward, the clivus makes a sharp angle with the dens epistrophei; the connection between the third and fourth ventricle, formed by the aqueduct of Sylvius, is an angulated one, and the elevated intracranial pressure from above easily closes the aqueduct by pressing the surrounding nerve tissue against the bony base (clivus).

The only way to open the passage for the fluid in the third ventricle, which is under the high pressure, is to bend the head backward, thus

bringing the clivus to the level of the dens, and reducing resistance to a minimum. The third ventricle will now act as a funnel above the aqueduct, and the fluid can more easily be pressed through the aqueduct. This bending of the head backward occurs oftener than we realize. If we ask patients with tumors above the tentorium about it, they will often say that pain in the forehead is relieved when they bend their heads backward.

Conditions are different in the skull, with tumors situated in the posterior fossa. In the majority of these cases, the aqueduct, the superior part of the fourth ventricle and the other ventricles are dilated.

Fig. 11 (Case 11).—Anatomic specimen from boy in Figure 10.

Bending the head forward cannot then alter these relations. The danger here lies in two factors which usually operate together, namely: (1) the direct pressure of the tumor on the medulla oblongata, and (2) the discharge of the fluid from the fourth ventricle into the cisterna cerebello-medullaris.

If we examine the relations in the posterior cranial fossa, it is obvious that in those cases in which by elevation of the cerebellum from the medulla oblongata or by enlargement of the cisterna cerebello medullaris the communication of the fourth ventricle with the exterior is opened again, there is good reason for the forward position of the head.

If the closure of the ventricle is due to complete filling of the ventricle by the tumor or by the cerebellum, moving of the head gives no change, and the patient will not experience the least relief by it. In these cases, the forced positions fail to appear.

Generally in such cases, the moving backward of the head will still be unpleasant, the edge of the foramen magnum compressing the medullary tumor. The head may also be bent backward in cases of tumors in the posterior fossa growing into the aqueduct (Figs. 10 and 11, Case XII).

That this danger is not imaginary, every experienced neurologist knows from the sudden deaths which occur during abrupt movements of the head. It cannot be accidental that after small doses of morphin in cases of ventricular tumors, cessation of the respiration occurs. The pain and the unpleasant sensations caused by ventricular tumors must be considered as danger symptoms and should not be disregarded.

CONCLUSIONS

Keeping in mind what has been noted above, I come to the following conclusions:

1. It is not justifiable to blame the forced positions of the head in cases of cerebral tumors on disturbances of innervation.

2. Mechanical factors will explain these positions.

3. For a correct understanding of these forced positions, the physiology of the movements of the head must be taken into account.

4. Disturbance in the discharge of the ventricular fluid plays an important part in the origin of the forced positions.

5. The diagnostic value of these forced positions is great.

6. In cases of supratentorial tumor, the patient moves his head backward. The fluid can then flow more easily out of the third ventricle, and the medulla oblongata does not then rest on the dens epistrophei.

7. In cases of subtentorial tumor, the patient will, in suitable cases, keep his head forward to enlarge the communication of the fourth ventricle and cisterna, to enlarge the cisterna and to free the medulla oblongata from pressure.

8. Tumors in the posterior fossa which grow in the direction of the aqueduct can sometimes cause a retracted position of the head.

SOME OBSERVATIONS ON THE SELF-STIMULATION HABITS OF YOUNG WILD ANIMALS*

CURT P. RICHTER, PH.D.

BALTIMORE

During the past summer in Panama I had opportunity to make a few observations on several forms of self-stimulation habits of three wild animals: a coatimundi, a kinkajou and a spider monkey. I had become accustomed to consider self-stimulation habits as confined to the human race in the form of thumb and finger sucking and erotic habits. It was therefore of considerable interest to observe these habits in young wild animals, all of which had started their lives in the jungle. It may be that some of our difficulties in understanding such self-stimulation habits in human beings are due to failure to consider their general biologic setting. It is hoped that the present limited observations may stimulate an attack on these problems from a more biologic point of view.

The first animal was a young female coatimundi. It belongs to a group called "small bears" by the Germans. These animals have some of the characteristics of bears but are often mistaken either for raccoons or, because of their long noses; for ant-eaters. They are, however, much higher developed than the latter. Their curiosity is scarcely equaled by that of monkeys. They poke their long noses into everything, and their prehensile feet are able to manipulate and investigate things with the greatest agility.

My coatimundi had been caught in the jungle when about 3 months old, taken to the home of Mr. Molina of David (who gave it to me) and given the freedom of the patio. It seemed to get along very well under conditions of semicaptivity and made no effort to escape.

It was while taking the four day boat trip from David to the Canal Zone with the coatimundi that I observed its peculiar habit of taking its left knee into its mouth and sucking and chewing it. At first I thought this little more than a cleansing habit, but I found that it occurred regularly when the coati went to sleep, was hungry or was thwarted in attempts to explore its surroundings, and especially when it became entangled in its ropes (Fig. 1). When given its freedom or when played with, the sucking activity immediately stopped. The indulgence was so frequent that the hair was almost completely worn away from the part of the knee that the coati took into its mouth.

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Observations over several months have shown that this special form of self-stimulation always occurs when the animal is going to sleep, but disappears whenever it gains its freedom and is able to forage in the ground and look for beetles. No effort has been made to break the habit.

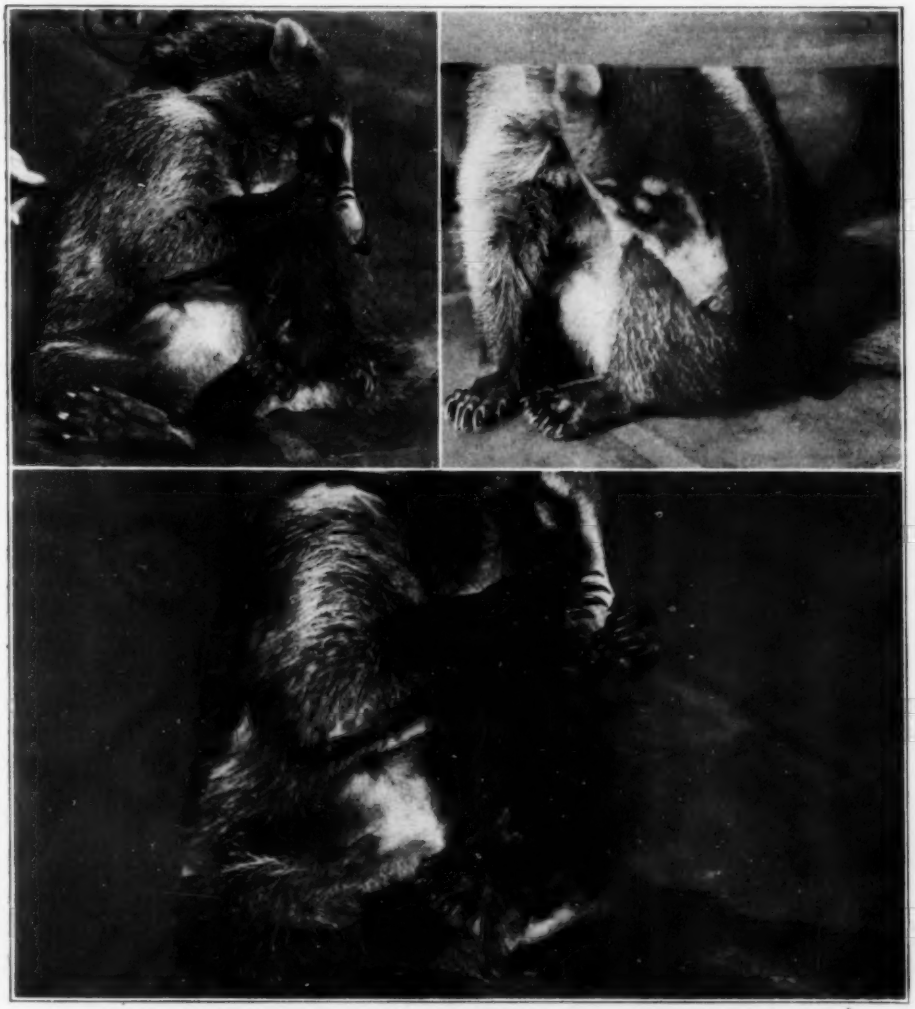

Fig. 1.—Several typical knee-sucking postures of the coatimundi.

The second animal was a male kinkajou, about 3 months old. The kinkajou is closely related to the coatimundi, but looks like a cross between a bear, a monkey and a cat. The picture of my young kinkajou is shown in Figure 2. Because of its supposed great predilection for honey it is often known as a honey bear.

This young kinkajou had been captured in the jungle shortly after birth, and had been brought up on a bottle by a physician. At 3 months of age, it had a habit of autofellatio so firmly fixed that the physician was unable to break it. This habit, like the knee-sucking of the coatimundi was indulged in when the animal went to sleep, when it was hungry or when it was thwarted in any of its activities. The act was made possible by the extreme flexibility of the neck and trunk of the animal. When it was curled up, the head was in close contact with the abdominal wall. The penis, which consists of a flap of skin about 1 cm. long, is situated unusually high on the ventral surface, so high that it might be mistaken for an abnormal formation of the umbilicus. When the animal is indulging in this activity, it is curled up into a perfect ball.

The third animal was a male spider monkey about 6 years old, which had been kept in the home of Dr. E. Currie in the Canal Zone since its capture in the jungle after the mother was shot. It was brought up on a bottle, its diet carefully regulated, and it was given a daily bath. When old enough it was permitted to eat at the table and to sleep with members of the family, and seemed to be perfectly adjusted to its human environment. It had always been well-behaved until the past year, when with the onset of puberty it occasionally showed entirely unprovoked outbursts of rage. In one of these, it bit its master rather severely so that it was given to me to be taken to Barro Colorado Island Laboratory on Gatun Lake.

On the way to the laboratory, I noticed that it sucked its fingers very much as many children do, especially when its activities were thwarted or when it was prevented from escaping. Sudden noises along the road or jarring of the car caused it to suck its fingers vigorously, and once during the trip it so fell asleep. The animal had had this habit since its capture, and no attempt had been made to break it. Unfortunately, the animal soon escaped.

This escape was interesting as illuminating the comparative strength of different cravings. When we reached the laboratory, the monkey was released a few feet from the edge of the jungle. It quickly made its way to the top of one of the tallest trees, where it dangled from one of the branches, making sounds of unmistakable joy. Then it suddenly turned and made its way through the treetops into the jungle, never to return. All of Dr. Currie's efforts to recall the animal with familiar calls and whistles were futile. A most firmly wrought attachment made during six or seven years of most intimate association with its master, and with marked dependency, could be dissolved without the slightest indication of a struggle by something

which the tall trees of the jungle offered; a something which, because of the previous condition of semicaptivity, this animal had never before experienced.

I should like to note that in all three animals the self-stimulation activity was sucking, but the area involved was different for each animal. It would seem that the sucking was the important thing, not the part of the body involved; that there is no reason to believe that the penis because it happened to be a sex organ played any different rôle in the kinkajou than did the knee in the coatimundi. It would appear to be a matter more of what part is most easily reached by the mouth and

Fig. 2.—Kinkajou.

how well this part fits the mouth. This factor is important in the knee-sucking of the coatimundi whose mouth is long and narrow and pointed. The sharp-edged flat knee fits it very well, and the lips of the animal everywhere are in close contact with it. The paws of the coatimundi with their sharp, nonretractile claws would not fit nearly so well as the knee. In the case of the kinkajou, the feet are considerably too large for the mouth and here, too, the sharp nonretractile claws would make it difficult to keep the paws comfortably in the mouth. In the spider monkey, the fingers of the hand are really the only parts of the body it can reach with its mouth and which can be left there

without danger of injury. The body, although more flexible than the human body, has still a limited scope of movement compared to that of the coatimundi or the kinkajou. Its mouth can reach only a few parts of its own body, and these parts happen to be so shaped that they are not suitable to be taken into the mouth. The fingers of the hand reach the mouth easily and also form a snug contact with the lips on all sides.

In discussing the origin of these habits, one must start with the all-important rôle played by the sucking habit. It is probably the most primitive of all mammalian habits. Preyer has observed the sucking activity in rabbit and guinea-pig fetuses and also in the human fetus. Schotti, Soltmann and Scheel also observed this activity in the human fetus. I have observed it in a number of rabbit fetuses about twenty days old. Because of the presence in utero of sucking activity, one must consider the possibility that self-stimulation sucking habits have their origin during this stage of the animal's development. I have made several observations on new-born human infants that seem to me to establish definitely the intra-uterine origin of these habits. In one infant especially, I noticed within one hour after birth, vigorous finger-sucking. There were blisters on the fingers that were sucked, and there was reason to believe that these blisters were raised before birth. This infant showed a well coordinated finger-to-mouth movement without the presence of random or trial and error attempts. I have learned from obstetricians that finger-sucking and thumb-sucking are observed occasionally in the first few minutes of postnatal life.

I believe that formation of these habits in utero depends, in the first place, on the ease and frequency with which the mouth comes into contact with the part of the body involved. The frequency of contact will depend largely on the activity of the fetus, the strength of the sucking activity itself will be a factor. Both the general bodily activity and the sucking activity will depend on the nourishment of the fetus. An under-nourished fetus will probably be much more active and suck very much more vigorously than a well-nourished fetus. Stimulation of the outside of the mother's body and the activity of the mother herself are also factors to be considered. It is my impression that most of these self-stimulation habits do have their origin in the intra-uterine stages of development, and that many which appear some time after birth are only to be regarded as revivals of earlier habits.

One important factor in the origin of self-stimulation habits of these wild animals is the fact that they were kept under conditions of captivity or semicaptivity without association with other animals of their own kind. The element of consolation probably played an important rôle here.

AN ATTEMPT AT A BIOLOGIC DIAGNOSIS OF STATES OF EXCITEMENT AND DEPRESSION *

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It is often difficult to make a definite diagnosis and prognosis in psychiatry, even after several days of observation. Indeed, some symptoms that are ordinarily relied on are to be found in psychoses of very different prognosis. For instance, certain kinds of manic patients who will eventually recover may present mannerisms, mutism, negativism, opposition to examination, stereotyped speech and attitude and apparent manifestations of inaffectivity. On the other hand, dementia praecox patients may present an excitement comparable to that of manic patients, with disturbance of attention, mobility of ideas, rapid association and apparent hyperamnesia, and yet may show, behind this excitement, a real affective and intellectual deficiency.

The prognosis may also be difficult to determine in the case of depressed patients. Is it a manic-depressive depression from which the patient will recover? Is it a depression symptomatic of dementia praecox? Or is it one of the asthenias, the evolution of which is always doubtful? Such problems occur every day in psychiatric practice, and are seldom solved. Yet the first question the relatives of the patients ask is: "Will the patient recover?"

It is often true also that in internal medicine one may be unable to give an accurate diagnosis, even after a thorough clinical examination. But the clinician will usually obtain some information from the laboratory that will lead him to a correct diagnosis. At the present time, there is a tendency in psychiatry toward biologic investigation. The study of serologic reactions in general paralysis and cerebral syphilis has shown the value of laboratory researches for diagnosis and prognosis in certain psychopathic states. A positive and irreducible serologic syndrome in the cerebrospinal fluid aids greatly in determining the existence of general paralysis.

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* Researches made at the Clinic for Mental Diseases.

* Read before the American Medical Society of Paris.

Neurologic signs and localizing symptoms enable one to be precise in the diagnosis of organic dementia. Measurement of the tension of the cerebrospinal fluid and radiography also give valuable information.

The application of these biologic methods to psychiatry is in its first stages. Researches carried out during several years at our clinic with a large number of functional psychoses have revealed the existence of important disturbances of the vagosympathetic equilibrium. Eppinger and Hess, in their well known memoir, brought out a considerable number of facts observed in psychopathic subjects. We have studied the neurovegetative tonus in normal persons, in patients suffering from general diseases, and in psychopathic subjects. We have been struck by the observation that states of great neurovegetative loss of balance, as well as states of complete atony, seem to occur especially in patients suffering from mental disorders. It is indeed common in certain patients to observe a considerable excitability of the vagus or of the sympathetic nerve, or even of the two together. The clinical signs, the pharmacodynamic tests and the visceral reflexes give responses of an intensity such as is not to be found elsewhere than in the psychopathic wards.

We have studied systematically the functional state of the neurovegetative system of more than 600 patients suffering from various mental disorders. Some of them have been followed for years, and our present material consists of several hundred pharmacodynamic tests and of about 6,000 graphically recorded tests. From these we believe it possible to build certain syntheses, especially since our results are absolutely homogeneous.

Starting with the study of the vagosympathetic disturbances in manic-depressive psychoses, we succeeded in ascertaining the existence of intense neurovegetative loss of balance and of variations in the vagosympathetic tonus paralleling the mental disturbances not only in manic excitement and in depression, but also in most psychoses that develop in attacks, the attacks being separated by periods during which the patients return to normal activity. It seems as if there is a link between the appearance of the morbid periods and exaggeration of vagosympathetic imbalance; the latter often precedes the appearance of the mental disturbance. One may even consider the possibility of a relation of cause and effect between the appearance of an abnormal vagosympathetic excitability and the development of morbid paroxysms. Indeed, in some patients, we have been able to delay or check the appearance of a periodic mental disturbance by checking the loss of balance in the vagosympathetic system. This may be due to the fact that in the pathogenicity of certain mental disorders there are disturbances of the exchanges of the cortical cells. The intensity and rapidity of these exchanges seem to be proportionate to the excitability of the vegetative

system, probably through the intermediation of a humoral or endocrine mechanism. It is not astonishing, therefore, if a characteristic state of the neurovegetative system is to be found constantly in the organic symptomatology of certain psychoses.

We shall pass rapidly in review the different categories of psychoses in which we noticed an abnormal state of this system.

MANIC-DEPRESSIVE PSYCHOSIS

The physical signs commonly observed during attacks of excitement and of depression mostly show an abnormal state of the neurovegetative system. The beginning of the attack is often marked by headache, poor appetite and constipation; the pulse is more rapid and the blood pressure modified; mydriasis and pupillary inequality often reveal a special condition of the tonus of the iris musculature; secretions are nearly always increased, especially salivation and sweating. Lastly, we observed, in the hours preceding the paroxysm, leukopenia with inversion of the leukocytic formula, recalling Widal's hemoclastic shock.

Clinical observation of the different forms of periodic psychoses reveals, therefore, the existence of a fairly deep disturbance of the vegetative life. The more precise study of the vagosympathetic tonus by means of pharmacodynamic tests, oculocardiac reflex, solar reflex, digestive hemoclasis and alimentary glycosuria tests has enabled us, after examination of more than 200 patients, to reach clear conclusions.

The anxious or manic paroxysms are characterized by a considerable hyperexcitability of the vagus, while on the contrary, there is a *relative* hypovagotonia during the intercalary periods. We stress the word "relative" as, generally, with cyclic patients, even in the intercalary periods, there is an abnormal excitability of the vagus. This is evidently considerably less in the same patient during the periods of quiescence than during the periods of manic excitement or anxious agitation. Intense oculocardiac reflexes are frequently to be observed during paroxysms. They are revealed, after compression of the eyeballs, by the change from a rhythm of 80 pulsations to one of 20 or even less per minute. The excitability of the vagus is such that simple compression brings an immediate decrease in the rate of the pulse, which stops often for more than six or seven seconds, and may sometimes produce a tendency to syncope.

The solar reflex is generally absent or inverted. Sometimes it appears at the beginning of or during the intercalary periods.

Reactions to pilocarpin or to eserin are marked. Inversely, with cyclic patients in a state of paroxysm enormous doses of atropin (from 3 to 4 mg.) must be used to cause paralysis of the vagus. These patients also tolerate suprarenal extract well.

Finally, during the paroxysms, the digestive hemoclasis test is always positive. Whereas, during the intercalary periods, variations of the leukocytic formula are generally small, leukopenia following a meal is marked and rapid. The hemoclastic cycle is completed in less than thirty minutes.

A remarkable tolerance to carbohydrates is observed at the same time. We frequently saw a tolerance limit of 150 gm. during the period of quiescence rise to 250 and sometimes 300 gm. during the phases of disease.

If the vagosympathetic state in these intermittent cases is followed regularly during intercalary periods, the end of these periods is always marked by: a progressive increase of the oculocardiac reflex, the disappearance of the solar reflex, the appearance of marked reactions to pilocarpin and eserin, a considerable tolerance to atropin and carbohydrates and a positive hemoclastic reaction; in short, by a progressive increase of the parasympathetic excitability. Vagotonia often precedes the attack by several days. By such observations we have been able, in some patients, to foresee the appearance of an attack when there was nothing clinically to indicate it.

This hyperexcitability of the parasympathetic which is always to be observed in manic or depressive attacks, was also noted distinctly in the course of mixed states belonging also to the periodic psychoses.

EPILEPSY

Similar variations of the neurovegetative tonus are also to be found in epileptic patients. Between the fits, we noticed either parasympathetic hyperexcitability or hypovagotonia. A distinction must be made according to the frequency and the repetition of the fits. In certain cases, we noticed, as Lesieur, Vernet and Petzetakis had done, a considerable exaggeration of the oculocardiac reflex, but we also observed considerable variations of this reflex; in particular, we saw the vagotonia increase in the days preceding the fit.

With the increased oculocardiac reflex in epileptic patients we generally noticed an inverted solar reflex, rapid and often intense digestive hemoclastic reaction, and sharp reactions to certain pharmacodynamic agents like eserin and pilocarpin. On the other hand, these patients tolerate fairly well atropin and suprarenal extract, which must be used in large doses to obtain distinct neurovegetative modifications. Finally, glucose tolerance is marked in these patients, being frequently higher than 200 gm. With other epileptic patients, particularly those who have few fits or periods of fits, we, on the contrary, generally noticed hypovagotonia or even sympathicotonia between the fits or periods of fits. The oculocardiac reflex is absent, or inverted, the solar reflex often

positive. Leukocytosis is always noted after a milk meal. The patient shows great sensitiveness to suprarenal extract and atropin, while reactions to pilocarpin and eserin are relatively weak. Sugar tolerance is not high, and the patient very often shows alimentary glycosuria after the injection of 100 to 120 gm. of glucose.

Before the fits there was always either exaggeration or the appearance of the oculocardiac reflex. In some patients, the oculocardiac reflex becomes positive and increases for several days before the fit, becoming more and more exaggerated until the fit begins. In other patients, the oculocardiac reflex is positive just a few hours or even a moment only before the fit. At the same time one notices disappearance or more distinct inversion of the solar reflex. Digestive hemoclasis is always positive as evidenced by a rapid and often accentuated leukopenia; sugar tolerance increases considerably, and reactions to eserin and pilocarpin become marked.

The appearance or exaggeration of the parasympathetic excitability has enabled us many times to foresee the occurrence of a fit or an equivalent.

During the fit we observed signs of hypertonicity of the vagus. In particular, at the very beginning of the fit, volleys of extrasystoles and cardiac contractions occurred. At the beginning of the fit there is also spontaneous leukopenia with an inverted leukocytic formula, as has been noted by Pagniez and Lieutaud, Bouché and Hustin, Dide and Guiraud, and, at the same time, signs of peripheral vasoconstriction.

In the minutes immediately following the fit one notices inversion, or a tendency to inversion, of the neurovegetative tonus. The oculocardiac reflex decreases, disappears or becomes inverted; the solar reflex is often positive. This state of parasympathetic hypotonicity is of variable duration. In some patients, this phase is short, and the oculocardiac reflex again becomes strongly positive. This happens especially in patients who frequently have fits.

The conditions observed in epileptic patients with convulsive manifestations may also be noted in patients presenting equivalents of psychic excitement, depression or a confusional state. In excited or anxious epileptic patients, hypervagotonia is the rule. On the other hand, in confusional states one generally observes relative hypovagotonia.

EMOTIONALLY UNSTABLE PATIENTS

As was to be foreseen from clinical observation, emotionally unstable persons show constantly a considerable excitability of the sympathetic system. In addition to intense vasomotor reactions and tachycardia, which indicated cardiovascular instability, a strong solar reflex is observed, with diminution and sometimes almost complete disappearance

of the oscillations. If the Pachon oscillometer without the graphic method is used, compression of the epigastric region determines a total disappearance of the oscillations of the index. The pilomotor reflex is often marked.

The injection of suprarenal extract (1 mg.) in these patients determines sharp reactions accompanied by painful sensations, anguish, horripilation, fine sweating of short duration, trembling and mydriasis. We have several times been able to note, after compression of the solar region of some of our emotionally unstable patients, the appearance of symptoms similar to those mentioned, which resemble the results of stimulating the suprarenal glands, determining, as Gautreley showed experimentally, a discharge of suprarenal extract.

Injection of atropin in these patients is often badly tolerated; the mouth rapidly becomes dry, the pupil dilates and the pulse becomes small and extremely rapid. Pilocarpin and eserin are not always well tolerated, probably because of their amphoteric action.

Digestive hemoclasis is difficult to investigate because of the patient's hyperemotivity. Indeed, one always notices leukopenia, linked probably with a peripheral vasoconstriction, due to the emotional reaction. On the other hand, the sugar tolerance test determines alimentary glycosuria with rather small doses.

This hypersympathicotonia may also be observed in certain psychoses associated with hyperemotivity, such as mania with anger and affective melancholia in certain states of anxiety. This was ascertained from the first researches made on the solar reflex (Thomas and J. C. Roux; H. Claude; Santenoise and Abaly).

In several cases of emotional confusion, a rare form of psychosis, it seemed to us that the patients also presented hypersympathicotonia.

MENTAL DEGENERACY

Degenerates, studied clinically so thoroughly by Magnan and his pupils, present, as is well known, in addition to their peculiar mental state, morbid outbursts, fits of delirium, episodic syndromes, obsessions, impulses, inhibitions, phobias, etc., which frequently justify their internment. These morbid states begin generally rather bruskly and end in the same manner. After them the patients are frequently released and returned to social life, where they may manifest a useful and often normal activity, though they remain strange, odd or disharmonious.

The observation of more than 150 patients of this kind, some of them followed for many years and during successive internments, revealed to us that the episodic syndromes seem to be under the control of a neurovegetative imbalance. In addition to their mental degeneracy, a factor in their constitutional psychic loss of balance, these patients

present a real neurovegetative dysfunction, a physical stigma which we were often able to trace in their ascendants, descendants and collaterals.

(*a*) *Delusional Outbursts.*—These are always accompanied by considerable vagotonia. One generally notices, at the same time, hyperexcitability of the sympathetic, especially in the outbursts of passionate type. The oculocardiac reflex is strongly marked, the solar reflex is often clear, and reactions to eserin and pilocarpin are sharp; sugar tolerance is increased, though often less than in manic excitement or pure depression.

(*b*) *Obsessions, Impulses and Phobias.*—These episodic syndromes are characterized by hypertonicity of both systems. Just as the beginning seems marked by an increase of the vagus excitability, so one observes with amelioration of the mental disturbances a distinct diminution of the excitability. The excitability of the sympathetic is also variable. One seldom observes, however, complete disappearance of the solar reflex. All these patients react fairly sharply to the different pharmacodynamic agents. However, by using inhibitors of both systems, so as not to determine a relative increase of one antagonistic system by the paralysis of the other; the tolerance to pharmacodynamic agents can be increased, and one can even obtain favorable effects from a therapeutic point of view.

(*c*) *Intermittent Perversions.*—We observed the existence of a neurovegetative instability in certain patients who periodically presented intermittent manifestations of instinctive perversion, periodic, one might even say paroxysmal, mythomania, fetishism and wickedness. Here again there was a distinct hypervagotonia, and sometimes also hypersympathicotonia. We have published the case of a young patient who presented a distinct parallelism between the manifestations of perversion and the appearance of hypertonia of the vagus.

(*d*) *Toxicomania.*—In drug addicts, one often finds symptoms of neurovegetative imbalance. These symptoms increase considerably during the withdrawal of the drug. Withdrawal in our experience was accompanied by marked hypertonicity of the vagus and often by the appearance of the solar reflex. When there is deception and the patient continues to use the drugs without the physician's knowledge, disappearance of the reflexes will attract the latter's attention and lead him to suspect the good faith of his patient.

CHRONIC SYSTEMATIZED DELUSIONAL STATES (PARAPHRENIA)

We found that the reactions of the neurovegetative system recalled those observed in normal people. The oculocardiac reflex, generally positive, was indicated by a slowing of from 10 to 12 pulsations per

minute; the solar reflex was generally absent, insignificant or inverted; reactions to various pharmacodynamic agents were of normal type. A meal was followed by digestive leukocytosis, and sugar tolerance was generally normal.

In addition to the psychoses in which sharp reactions on the part of the neurovegetative system are to be found, a whole group of psychoses, not yet homogeneous, in which neurovegetative reactions are transitorily or permanently absent, must be mentioned.

MENTAL CONFUSION

Experimentation has shown that in the presence of an intoxication the organism reacts by an inversion of the neurovegetative system. When the toxin has been eliminated and the cause of the intoxication has disappeared, the tonus returns to its former state.

We, therefore, have not been surprised to note in the study of sixty cases of mental confusion that the reactions of the neurovegetative system were only slightly marked in toxic psychoses. Whether the case was a confusional state secondary to an exogenic or endogenic intoxication, a toxi-infectious psychosis, an acute delirium or a state of stupor, or a clinical picture of either typical mental confusion, depression or a mixed state, when the psychosis was consecutive to an intoxication, the same type of neurovegetative reaction was found. The oculocardiac reflex was not marked and was generally absent; the solar reflex was frequently though not constantly positive; the patients presented insignificant reactions to all kinds of pharmacodynamic agents.

After a few days, when the signs of intoxication had disappeared, namely, the signs of a confusional order, there frequently appeared an important excitability of the vagus which increased while these symptoms were disappearing.

ASTHENIA

The symptomatology in some patients is constituted solely by an incapacity for any effort and extraordinary fatigability, without any sign of suprarenal insufficiency. Most often we found in these patients an atony of the neurovegetative system. The oculocardiac reflex and the solar reflex were absent, tolerance to carbohydrates was much diminished, and there was only a slight variation of the leukocytic formula after meals.

One must, however, distinguish two types: (1) Some patients, whose asthenia is generally transitory with a favorable prognosis, seem to react, at least slightly, to pharmacodynamic agents. Eserin, pilocarpin and suprarenal extract determine the appearance of a slight oculocardiac reflex and of a small solar reflex. (2) In other patients, the neuro-

vegetative system remains atonic, notwithstanding the use of pharmacodynamic agents. The patients of this type whom we observed have remained in the same state of areflexia. Prognosis appears to be more doubtful with these patients than with the first type, and there is some question whether their condition will not evolve into dementia praecox.

DEMENTIA PRAECOX

Dementia praecox in young people, both in the hebephrenic and hebephrenocatatonic forms (the patient being calm or agitated), has always exhibited a fixed neurovegetative syndrome characterized by atony of the neurovegetative system, which has hitherto proved irreducible. The oculocardiac reflex is absent, the solar reflex is most often absent, tolerance to carbohydrates is not marked, and alimentary glycosuria may even be observed after meals despite an apparently normal state of the hepatic function. Leukocytic variations consecutive to meals are slight, and a mild leukocytosis is sometimes noticed. Accidents due to administration of serum are never observed. The injection of pilocarpin, eserin, atropin and suprarenal extract does not generally determine any reaction or variation of the pulse or of the blood pressure. Blood pressure is usually low and the oscillometric index small.

This irreducible atony of the neurovegetative system seems to us quite characteristic of true primary dementia praecox as French authors understand it (Morel, Christian). We observed these facts both in the simple forms and in the forms with excitement and depression as well as in the form similar to the mixed states. We observed this syndrome in young people whose disease had appeared without cause and also in three cases of postencephalitic dementia praecox.

COMMENTS

From our observations, it is possible to group the psychoses according to the neurovegetative reactions in five large categories: (1) those which show hypervagotonia, (2) those which show hypersympathicotonia, (3) those which show hypertonicity of both systems, (4) those in which the neurovegetative reactions are normal, and (5) those in which reactions are absent, either transitorily or permanently.

The accompanying table summarizes these results. It is not a classification but a schematization.

How can these views be applied to the diagnosis of states of excitement and depression? As has been shown, the diagnosis, and consequently the prognosis, of states of excitement and depression is among the most delicate problems of psychiatry, especially when the appearance of the patients is even slightly atypical.

Schematic Presentation of Psychoses According to Neurovegetative Reactions

Vagotonia	Sympathicotonia	Neurotonia Vagotonia + Sympathicotonia	Normal Neurovegetative Reactions	Hyponeurotonia		
				Temporary	Modifiable	Irreducible
Oculocardiac reflex = +	Oculocardiac reflex = 0	Oculocardiac reflex = +		Oculocardiac reflex = 0	Oculocardiac reflex = 0	Oculocardiac reflex = 0
Solar reflex = 0	Solar reflex = +	Solar reflex = +		Solar reflex = 0 or +	Solar reflex = 0	Solar reflex = 0
Sharp reactions to eserin and pilocarpin	Sharp reactions to suprarenal extract and atropin			Appear after a few days	Appear after use of certain pharmacodynamic agents	Nothing modifies this state
Tolerance to atropin						
Tolerance to glucose	Weak tolerance to glucose					
Manic-depressive: Mania	Emotionally unstable	Degenerates				Prolonged asthenia
		Outbursts of delirium	Various systematized delusional states			
Manic-depressive: Depression				Intoxication psychoses	Temporary asthenia	
Mixed states	Mania with anger	Obsessions Impulses				
	Affective melancholia					
	Emotionally unstable with anxiety	Intermittent instinctive perversions				
	Emotive confusion	Toxicomaniacs				
Epilepsy: Convulsive attacks						Dementia praecox
Epilepsy: Equivalents: Excitation						
Epilepsy: Equivalents: Depression						

As will be observed from the accompanying schema, characteristic differences exist in the states of excitement and depression occurring in the different forms of psychoses. Roughly speaking, it seemed to us that the mental disturbances that appear in the form of attacks and are separated by relatively normal periods were most often accompanied by hypertonicity of the vagus, or of both vegetative systems. On the other hand, in patients, such as those with dementia praecox, in whom the clinical manifestations depend on a psychosis with chronic evolution and consequently of unfavorable prognosis, we always noticed feeble or negative types of vagosympathetic reactions. These observations may prove useful for diagnosis.

States of Excitation.—In the presence of a state of excitation, one may consider:

1. A state of true manic excitement, belonging to the manic-depressive group, for which one can foresee recovery from the attack. In this case, one will invariably find distinct hypertonicity of the vagus unless there is a marked alcoholic influence, in which case the results may be hidden for several days because of the reaction of the organism to the intoxication.

2. A state of manic excitement linked with an emotional process, as in mania with anger. One finds then solely a hypertonicity of the sympathetic.

3. A state of excitement linked with an intoxication: (*a*) In drug addicts before withdrawal, the neurovegetative reactions are absent, but the reflexes appear strongly as soon as the drug is stopped; (*b*) in alcoholic intoxication in the acute or subacute forms, reflexes are absent, but they reappear as soon as the confusional state ceases; (*c*) in psychoses due to endogenic intoxication, the reactions are of the same order.

4. A state of excitement in dementia praecox. In this case, the neurovegetative system presents a complete and irreducible atony.

The problem of the diagnosis of states of excitement is often complicated by the existence of a certain number of added delusional ideas: (*a*) In intermittent manic attacks ideas of influence are often observed, as Logre and Heuyer showed; in these patients, the oculocardiac reflex is strongly marked, the solar reflex is generally inverted, and the sugar tolerance is high. (*b*) In degenerates with weak constitutions, the outbursts of delusion formation are known often to be accompanied by a state of excitement; in such cases we observed a distinct hypertonicity of the sympathetic. (*c*) In dementia praecox, the polymorphous, unsystematized delusional states are also extremely frequent, but here the neurovegetative reactions are absent.

We have been able in certain cases to make a diagnosis based solely on biologic findings, even when the clinical signs were rather in favor of a different diagnosis. The later evolution always demonstrated that we were right.

States of Depression.—In the presence of a simple state of depression without delusional ideas, one may think of: 1. A state belonging to the manic-depressive psychoses. In this case the hypertonicity of the vagus is characteristic.

2. A confusional state. Here the reflexes are not marked, but they reappear when the causes of intoxication disappear.

3. Temporary asthenia. In this disorder, the vagosympathetic reactions are not marked; they appear after the use of pharmacodynamic agents.

4. Dementia praecox, particularly dementia praecox of young people. The atony of the neurovegetative system is irreducible.

States of Anxious Agitation.—When the dominating symptom is an anxious agitation with or without delusional ideas, the case may be:

1. A depression or a manic state belonging to the manic-depressive psychosis.

2. A state of emotional instability with hypersympathicotonia.

3. A confusional state.

4. An episodic symptom of degeneracy: obsessions, impulses, phobias.

5. Dementia praecox.

To each of these states there is a corresponding vagosympathetic formula.

To depression and anxiety are often added delusions. They may occur:

1. In intermittent insanity. Delusions develop consecutive to a moral grief.

2. In affective depression. The delusions are linked with a state of anxiety of psychogenic origin, and develop on a soil of hyperemotivity with hypersympathicotonia.

3. In degenerates. Here one can find delusional formations with depression in the course of the outbreaks and of the various episodic syndromes.

4. In dementia praecox. Patients frequently show delusional ideas of a melancholic type.

In these different forms, diagnosis and prognosis can be facilitated by the examination of the neurovegetative tonus. In a depressed patient

who has apparently given up his delusion, the finding of a sharp solar reflex would lead one to apprehend anxious reactions with attempts at suicide. Such patients, therefore, must still be carefully watched.

CONCLUSIONS

The systematic examination of the neurovegetative tonus in a great number of psychopathic subjects has enabled us to find, in many of them, considerable disturbances of the vagosympathetic activity. Studying the problem more closely, we observed that certain vagosympathetic formulas corresponded to certain psychoses and were almost characteristic of these diseases. In certain patients, we constantly found hypervagotonia; in others, hypersympathicotonia; others showed hyperexcitability of both systems. Finally, some showed a temporary atony of the neurovegetative system, others an irreducible atony.

In certain difficult cases the orientation of our diagnosis was accurately directed with the aid of these biologic data. We have thus been able to group with either the periodic psychoses, mental degeneracy, states of constitutional hyperemotivity, intoxication psychoses or dementia praecox, certain atypical states of excitement or depression when the clinical examination did not enable us to reach definite conclusions.

Among the many means of investigating the functional state of the vegetative nervous system, those which have given us the most accurate and the most constant answers are the oculocardiac and the solar reflexes. These procedures are simple and they can be carried out by any practitioner. It is not always easy, however, to detect them in excited, anxious or rebellious patients. For that reason, we have looked for another method of examination which may be applicable to all patients.

We chose the alimentary glycosuria test used by Lewis and Benedict and by Naunyn in the investigation of hyperthyroidism. We have observed with it an extremely high tolerance of vagotonic patients to carbohydrates. We administer from 1.8 to 2 gm. per kilogram of body weight. If this dose is tolerated, the patient is vagotonic. The test is then repeated, the dose being increased. From 200 to 250 gm. can thus be given to certain patients. If, inversely, after the ingestion of the first dose, sugar is found for several hours in the urine, it shows that the patient is not markedly vagotonic. The test is then repeated and if, by diminishing the quantity of glucose administered, glycosuria is still found, it means that the patient is hypovagotonic. Naturally this test has value only in patients with a normal liver.

In sympathicotonic patients, the great sensitiveness to suprarenal extract will also give useful information.

By this method, with all patients, whatever their opposition to examination or their agitation, one can secure as much information concerning the neurovegetative tonus as with the use of certain pharmacodynamic agents. This information, we believe, will enlighten the clinician on the diagnosis and the prognosis of the disease.

BLOOD IN PERSONALITY DISORDERS

BIOCHEMICAL STUDIES

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Since there still exists considerable uncertainty concerning the relationship of certain constituents of the blood to the various personality disorders, another [1] report of the findings of this laboratory seems justifiable. Included in this report is a special study of the carbon dioxid combining power of the blood plasma, and of the urea nitrogen of the blood.

METHODS OF PROCEDURE

All specimens of blood were obtained within ten days after the patient had been admitted to the hospital. Blood for carbon dioxid determinations was taken by venipuncture before breakfast, twelve hours after eating, and while the patient was still in bed. Sodium oxalate was used to prevent clotting. The blood was allowed to flow directly into the tube containing the oxalate, with as little shaking as possible. The blood was centrifugalized, and the plasma was drawn off within from one-half to one hour after the blood had been collected, care being taken to have as little exposure to the air as possible. A comparison of tests run on blood collected under oil with those done in the manner described above gave essentially the same results, provided the tests were made soon after the specimens had been taken. Determinations of the bicarbonate content of the plasma were made according to the method of Van Slyke and Cullen.[2]

The nonprotein nitrogen, uric acid, sugar and chlorid determinations were made on the blood filtrates, according to the methods of Folin and Wu [3] and of Whitehorn.[4] Determinations of urea nitrogen were made

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1. Bowman, Karl M.: Blood Chemistry in Mental Diseases, Am. J. Psychiat. **2**:379 (Jan.) 1923.

2. Van Slyke, D. D., and Cullen, G. E.: The Bicarbonate Concentration of the Blood Plasma: Its Significance and Its Determination as a Measure of Acidosis, J. Biol. Chem. **30**:289, 1917.

3. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **38**:81, 1919; A Simplified and Improved Method for Determination of Sugar, J. Biol. Chem. **41**:367, 1920.

4. Whitehorn, J. C.: Simplified Method for the Determination of Chlorids in Blood or Plasma, J. Biol. Chem. **45**:449, 1921.

on whole blood according to the method of Van Slyke and Cullen,[5] nesslerization being used in preference to titration.

All blood chemistry examinations were begun within one hour after the specimens had been collected. The blood was collected, by venipuncture before breakfast, into tubes containing powdered sodium oxalate.

CARBON DIOXID COMBINING POWER

In recent years, it has been alleged that there is a reduction of the carbon dioxid combining power of the blood plasma of the mentally sick. In other words, it is claimed that there is defective oxidation of organic acids similar to that found in abnormal conditions such as diabetes, or that there is decreased elimination of acid substances such as occurs in nephritis. As a result, when the accumulation of these acids exceeds certain physiologic limits, nonvolatile acids combine with the carbonates, phosphates and alkaline protein compounds of the blood, so that the "alkali reserve" or carbon dioxid combining power of the blood plasma is reduced.

It is difficult to conceive of metabolic changes that could result from uncomplicated personality disorders and cause a reduction of the alkali reserve. Those psychoses due to or complicated by somatic diseases, toxins, infections or physical exhaustion might, however, show some reduction of the carbon dioxid combining power of the blood plasma. As no systematic study of this subject had thus far been made, determinations were made on the blood of 200 patients consecutively admitted to the hospital.

In these determinations, the normal findings (according to Van Slyke and Cullen) of from 53 to 75 c.c. of carbon dioxid per hundred cubic centimeters of blood plasma were used as standards for comparison. In each case, note was made of physical findings that might influence the amount of alkali reserve. From the case records were obtained the age, sex, diagnosis, other blood chemistry findings, results of urinalysis, blood pressure, leukocyte count, evidences of focal infection, temperature, pulse rate and respiration. Except in psychoses due to somatic disease, other blood chemistry findings were normal. The age, sex and blood pressure had no appreciable relation to the results. Nine patients had leukocytosis with slight elevation of temperature and showed an average carbon dioxid rate of 53.7, the minimum rate in these cases being 49 and the maximum 61.4. Fifty-four patients had one or more infected teeth, six had positive blood Wassermann reactions, one had amebic dysentery, one had tuberculosis, one had furunculosis

5. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease and Its Use for Rapid and Accurate Determination of Urea, J. A. M. A. **62**:1558 (May 16) 1914.

and one had a mild grade of nephritis. In this group of patients, the average carbon dioxid rate was 58.3, the minimum rate being 44.3 and the maximum 74.

It will be observed that patients with physical findings that suggested conditions in which the carbon dioxid rate might be lowered had an average rate within normal limits.

A grouping of the patients according to clinical diagnosis gave the following results:

TABLE 1.—*Volume Per Cent. of Carbon Dioxid*

Diagnoses	Number Examined	Minimum Rate	Maximum Rate	Average Rate
Manic-depressive depression	55	44.3	69.1	58.5
Manic-depressive excitement	34	51.9	73.0	61.2
Dementia praecox	27	49.0	74.0	56.9
Paranoid condition	16	48.1	67.2	55.0
Psychoneurosis	13	52.2	70.2	60.4
Psychosis with organic brain disease	11	49.0	68.5	57.4
Psychosis with other somatic disease	11	34.7	73.0	55.4
Drug addiction	11	51.9	68.1	58.8
Involution melancholia	8	53.8	61.7	59.3
Constitutional inferiority with psychosis	7	53.8	63.3	60.4
Constitutional inferiority without psychosis	5	58.1	61.4	60.0
Without psychosis	2	48.0	62.4	55.2

Total number of examinations, 200
Average carbon dioxid rate of all examinations, 58.4

These findings permit the conclusions that (1) the blood plasma of persons suffering from personality disorders uncomplicated by physical illnesses has normal carbon dioxid combining power, and (2) personality disorders accompanied by physical findings such as infected teeth, slight elevation of temperature (99 to 100 F.), moderate degree of leukocytosis (10,000 to 15,000), and either high or low blood pressure, do not on that account show any appreciable change in the carbon dioxid combining power of the blood plasma.

UREA NITROGEN

Routine urea nitrogen determinations were made on the blood of 143 patients consecutively admitted to the hospital. The results according to clinical diagnostic groupings were as follows:

TABLE 2.—*Urea Nitrogen Mg. Per Hundred Cubic Centimeters in Patients Examined*

Clinical Diagnosis	Number of Examinations	Minimum Rate	Maximum Rate	Average Rate
Manic-depressive depression	40	8.3	25.0	15.2
Manic-depressive excitement	22	10.0	31.3	15.0
Dementia praecox	13	8.9	22.7	14.4
Paranoid condition	12	11.9	25.0	15.2
Psychoneurosis	12	9.6	21.0	13.0
Psychosis with organic brain disease	9	11.6	25.0	16.2
Involution melancholia	6	12.9	31.3	20.7
Constitutional inferiority with psychosis	4	10.0	18.9	16.0
Constitutional inferiority without psychosis	3	10.8	15.6	13.2
Psychosis with other somatic diseases	11	8.3	46.0	18.5
Drug addiction	9	11.3	19.2	15.1
Without psychosis	2	10.0	19.0	14.5

Total number of examinations, 143
Average urea nitrogen rate of all examinations, 15.2

From these findings, it is seen that the urea nitrogen of the blood is unaffected in any personality disorder unless there is some definite complicating physical illness.

Since Bowman [1] reported on the nonprotein nitrogen, dextrose, uric acid and chlorids in the blood of 229 patients consecutively admitted to the hospital, examinations of these chemical constituents of the blood have continued to be made chiefly at the request of the clinical service. Since the results accord with those already reported, only a brief summary will be given.

Using these values as normal standards for comparison, the results in our examinations are given in Table 4.

TABLE 3.—*Normal Values Given by Four Different Authorities and Expressed as Milligrams Per Hundred Cubic Centimeters Whole Blood*

	Gettler and Baker	Folin and Denis	Myers and Fine	Hawk
Nonprotein nitrogen	20 - 45	22 - 37	25 - 30	25 - 35
Dextrose	50 -120	90 -100	90 -130	80 -110
Uric acid	1 - 3.5	0.7- 3.7	1 - 2	1 - 3
Chlorids, as sodium chlorid	450 -500	490	457	650

The normal values used at this hospital are essentially an average of these figures and are as follows: Nonprotein nitrogen, 24-35; dextrose, 80-120; uric acid, 1-3; chlorids, as sodium chlorid, 450-500.

TABLE 4.—*Comparison of Results in Authors' Examinations with Normal Standards in Table 3*

	Number of Examinations	Number Found Normal	Number Found Abnormal
Nonprotein nitrogen	334	319	15
Dextrose	431	393	38
Uric acid	348	347	1
Chlorids, as sodium chlorid	226	225	1

Of the fifteen nonprotein nitrogen determinations which were abnormal according to our values, twelve were within the normal limits as given by Gettler and Baker. Two of the other three patients had nephritis, and the third was a general paralytic who was critically ill at the time when the specimen was obtained, and who died three days later.

Of the thirty-eight patients whose dextrose determinations were beyond the limits according to our standards, ten had diabetes. The determinations in the other twenty-eight are reported briefly in Table 5.

None of the patients on whom the determinations in Table 5 were made had glycosuria.

The abnormal uric acid and chlorid findings, one of each, were both in cases of nephritis.

GLUCOSE TOLERANCE

Glucose tolerance tests were made on an unselected group of patients without reference to the clinical diagnoses. Blood for these determinations was taken before, and one, two and three hours after the ingestion of 0.8 gm. of glucose per pound of body weight, dissolved in 2 c.c. of water per pound of body weight. The juice of one lemon was added to make the meal more palatable. Since practically all patients showed the change in blood sugar content to remain essentially within the

TABLE 5.—*Results of Dextrose Determinations in Twenty-Eight Patients*

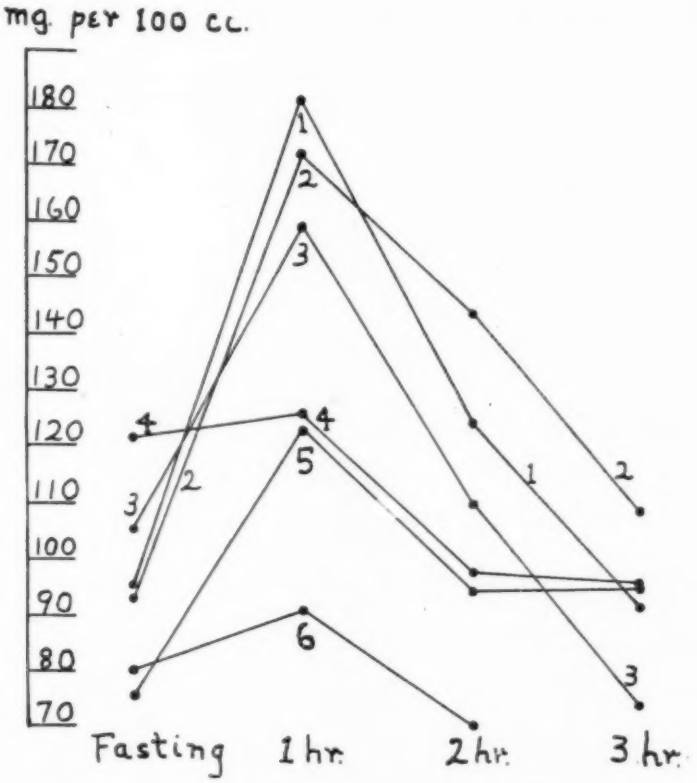
Diagnoses	Number of Examinations	Dextrose, Mg. per 100 C.c.
Manic-depressive depression	7	131, 142, 133, 143, 133, 130, 154
Manic-depressive excitement	1	129
Involution melancholia	3	142, 167, 133
Psychoneuroses	3	133, 143, 133
Dementia praecox	2	56, 133
Psychoses with other somatic diseases	5	133, 154, 128, 160, 132
Drug addiction	4	142, 138, 154, 166
Chronic alcoholism	1	133
General paralysis (critically ill)	2	182, 204

TABLE 6.—*Results of Examination for Glucose Tolerance*

Diagnoses and Number Examined		Glucose, Mg. per 100 C.c. Fasting	First Hour	Second Hour	Third Hour
Thirteen cases of manic-depressive depression	Minimum	80	118	87	52
	Maximum	133	315	200	133
	Average	96	182	124	92
Nine cases of dementia praecox	Minimum	83	111	91	74
	Maximum	105	266	193	171
	Average	94	172	143	109
Four cases of constitutional inferiority without psychosis	Minimum	91	111	67	91
	Maximum	136	139	133	106
	Average	121	126	98	97
Three cases of constitutional inferiority with psychosis	Minimum	87	125	91	60
	Maximum	121	200	125	87
	Average	106	150	110	74
Three cases of paranoid condition	Minimum	80	78	50	84
	Maximum	85	146	138	108
	Average	78	122	95	96
Three cases of psychosis with other somatic disease	Minimum	91	108	91	83
	Maximum	100	211	149	133
	Average	96	162	119	104
One case of epileptic psychosis		89	124	111	108
One case of psychosis with arteriosclerosis		71	80	71	...
One case of chronic alcoholism		77	143	108	77
One case of involution melancholia		125	234	200	111
The same patient in manic phase		80	91	70	...
and in depressive phase		82	119	102	93

normal limit in the third hour blood specimens, examinations of the blood three hours after the ingestion of the glucose were omitted during some of the later tests. The patients remained in bed without food throughout the period during which specimens were being obtained. None of these patients had any obvious physical illness or evidence of ductless gland disorder. In no case was glycosuria found during the twenty-four hours following the ingestion of the glucose meal. The results are given in Table 6.

Although the number of examinations was limited, a sufficient number of manic-depressive depression and dementia praecox cases were studied to indicate the character and rate of sugar metabolism in these disorders. All the patients with dementia praecox were in acute stages of the illness, and most of them were paranoid in type. It is interesting to note that the glucose curves obtained are similar to those



Glucose tolerance curves. Curve 1 indicates manic-depressive depression; Curve 2, dementia praecox; Curve 3, constitutional inferiority with psychosis; Curve 4, constitutional inferiority without psychosis; Curve 5, paranoid condition; Curve 6, manic-depressive excitement.

reported by Lorenz [6] and by Raphael and Parsons.[7] It would seem, however, that since neither affective nor dementia praecox psychoses have been shown to be associated with the dysfunction of any particular

6. Lorenz, W. F.: Sugar Tolerance in Dementia Praecox and Other Mental Disorders, Arch. Neurol. & Psychiat. **8**:184 (Aug.) 1922.

7. Raphael, T., and Parsons, J. P.: Blood Sugar Studies in Dementia Praecox and Manic-Depressive Insanity, Arch. Neurol. & Psychiat. **5**:687 (June) 1921.

gland, organ, or other part of the body, it would be better for the present to regard the glucose curves as characteristic of the general metabolic processes in these disorders. In other words, the glucose tolerance curves found in depressions and acute cases of dementia praecox indicate a definite retardation in glucose metabolism. In marked contrast to the retardation found in these disorders is the definite acceleration of glucose metabolism in cases of manic-depressive excitement.

These findings indicate definite changes in the function of the vegetative nervous system in certain psychoses. Further evidence of these changes are found in the recent observations of Farr and Lueders on secretory functions in the psychoses,[8] and the basal metabolism studies [9] and observations made in this laboratory of the motor functions of the digestive tract.[10]

CONCLUSIONS

1. Determinations of the carbon dioxid combining power of the blood plasma of 200 patients consecutively admitted to the hospital indicate that this combining power is unaffected by psychoses unless there is some definite accompanying physical disease.

2. Determinations of the urea nitrogen content of the whole blood of 143 patients consecutively admitted gave negative results.

3. Further studies of the nonprotein nitrogen, uric acid, dextrose and chlorid content of the blood of persons suffering from personality disorders corroborate the negative results reported by other observers.

4. Glucose tolerance tests show more or less characteristic changes in the glucose content of the blood of patients in either phase of affective psychoses and in the acute stages of dementia praecox. These changes indicate a definite retardation of functions of the vegetative nervous system in manic-depressive depression and in the acute stages of dementia praecox and an acceleration of these same functions in manic-depressive excitement.

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8. Farr, Clifford B., and Lueders, Charles W.: Gastric Secretory Functions in the Psychoses, Arch. Neurol. & Psychiat. **10**:548 (Nov.) 1923.

9. Bowman, K. M., et al.: Bio-Chemical Studies in Ten Cases of Dementia Praecox, Boston M. & S. J. **187**:358 (Sept.) 1922.

10. Henry, G. W.: Some Roentgenologic Observations of Gastro-Intestinal Conditions Associated with Mental Disorders, Am. J. Psychiat. **3**: (April) 1924.

REFLEXES OF DIFFERENT ORDER ELICITABLE FROM THE ABDOMINAL REGION *

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In a monograph on the abdominal reflexes,[1] I have pointed out that one cannot regard every reflex contraction of the abdominal wall elicitable from the abdominal region as identical with the normal cutaneous abdominal reflex.

First, there is a periosteal reflex of the costal margin, elicitable by percussion of the costal border a little mesiad to the mammillary line. This reflex consists in a contraction of the abdominal muscles—particularly the external oblique—with deviation of the umbilicus toward the point of percussion. This reflex is easily distinguished from the cutaneous abdominal reflex; in the great majority of cases, when the latter is abolished on account of pyramidal lesion, the former is found to be brisk—sometimes even distinctly exaggerated.[2]

More difficult to distinguish from the normal abdominal reflex is a reflex which is sometimes encountered in cases in which there can be no doubt that the pyramidal fibers are seriously affected—even in complete transverse lesions of the cord.

In the monograph alluded to, I ventured to suggest the possibility that the abdominal reflex, found by Déjerine [3] and Long in a case of complete transverse lesion of the cord, might have been a pathologic type of abdominal reflex. In 1921, I described a case of right hemiplegia, accompanied by a flexion reflex of the homolateral limbs [4] in which such an abdominal reflex was found. The following features distinguished this reflex from the normal abdominal reflex:

1. It appeared after a longer latent period (one or two seconds, varying according to the strength of stimulus).

2. The contraction of the abdominal muscles was markedly bilateral, and the muscles of the contralateral side would now and again contract more forcibly than the homolateral muscles, causing deviation of the umbilicus and the linea alba to the left.

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* From the Neurological Clinic of the Norwegian State University.

1. Om abdominalreflexerne, Christiania, 1918.

2. For the lower part of the abdomen, Guillain and Alajouanine have recently described a similar periosteal reflex—"Le réflexe médio-pubien." Guillain: V. réunion neurologique, Rev. neurol. 1924, No. 6, p. 652.

3. Déjerine: Semiologie, 1911, p. 968.

4. Monrad-Krohn, G. H.: Contribution to the question of a possible inversion of the abdominal reflex, Acta med. scandinav. **54**:603, 1921.

3. The contraction would sometimes be accompanied by slight flexion at the right hip and knee joint.

4. The stimulus required to elicit this bilateral reflex from the right side of the abdomen was much stronger than that required to elicit the normal abdominal reflexes from the right side.

5. The tickling sensation that accompanied the normal left abdominal reflexes was absent.

It will be agreed that in this case the abdominal reflex elicited would belong to the order of "reflexes of spinal (mesencephalic) automatism." The study of these reflexes will show that an abdominal contraction may be a more or less strongly accentuated component of this complex reflex response (as described by Babinski,[5] Riddoch and others), and when this abdominal component is strongly pronounced, the distinction may sometimes be difficult.

My assistant, Dr. Öwre, in a number of cases has mapped out the reflexogenous area for these reflexes of spinal automatism (the results will shortly appear in the *Videnskabs-selskabets skrifter*, Christiania), and it was found that confusion may readily arise if in eliciting the abdominal reflexes one does not take the reflexes of spinal automatism into account, as the reflexogenous area of these reflexes was often found to cover the abdomen to a greater or lesser extent.

The following two cases may be of some interest as they both presented abdominal reflexes of an undoubtedly pathologic type, yet at first sight resembling the normal cutaneous abdominal reflex to some degree.

CASE REPORTS

CASE 1.—The patient was admitted for the second time on April 4, 1924. The present illness began during the spring of 1922. He began to drag the right leg, which was rigid and weak. He was admitted to the neurologic section of Rikshospitalet, where he remained from August 19 to 22, under the diagnosis "paraparesis spastica" (without sensory loss). The plantar reflexes were inverted on both sides, and the deep reflexes were brisk. Patellar and ankle clonus were present on both sides. The abdominal reflexes were feeble, but nothing peculiar concerning them was noted. After the patient was discharged from the hospital, both legs gradually became weaker, and at the second admission he was able to walk indoors only by supporting himself by a walking stick and the furniture. On examination, mentality and the cranial nerves revealed nothing abnormal. There was distinct weakness accompanied by marked rigidity of both lower limbs—more pronounced on the right. The abdominal muscles also showed general paralysis accompanied by some rigidity. There was doubtful loss of sensation to superficial pain (pin prick) and temperature below the sixth dorsal segment and some indefinite loss of tactile sensation in the left lower abdominal region. All deep reflexes were brisk; patellar clonus and ankle clonus were present. The plantar reflexes were extensor. Pathologic flexion reflexes were present on both

5. Babinski: Refllexes de défense, Rev. neurol., August, 1922.

sides.[6] Lumbar puncture yielded clear fluid. Jugular pressure caused immediate rise of pressure of the fluid. The fluid showed slight increase in the number of cells and corresponding slight increase in the amount of proteins — otherwise nothing abnormal. The Wassermann reaction was negative both for the blood and in the fluid. The colloidal gold reaction showed slight discoloration at the dilutions of 1:40 and 1:80. When an attempt was made to elicit the abdominal reflexes, the abdominal wall contracted equally well on both sides — no matter which side was stimulated. This bilateral abdominal reflex was accompanied by extension reflex of the lower limbs, most pronounced on the side corresponding to the stimulus. This complex reflex response could be elicited equally well by application of cold or by faradization. The patient's condition has been the same for months.

Comment.—The case is probably one of disseminated sclerosis with a plaque in the upper dorsal region. There can be no doubt about the existence of a lesion in this region, even if its nature is doubtful.

The abdominal reflex found in this case evidently is one belonging to the group of "reflexes of spinal automatism." The points which distinguish it from the normal abdominal reflex are:

1. The reflex is always bilateral.
2. It is accompanied by an extension reflex of the lower limbs.
3. It may be elicited by cold as well as by stroking with a pin.

Case 2.—The patient was admitted to the hospital April 6, 1924. He had acquired syphilis twenty years before. He married in 1910, and had three healthy children. His wife, was in good health. In 1906, his kidneys were said to be affected. In the winter of 1922-1923, diplopia occurred and disappeared. In the autumn of 1923, his legs and arms gradually grew weak, and since December, 1923, he had been in bed. Later uncontrolled laughing and weeping for no adequate reason occurred. He was loquacious and unsettled and burst into laughter without cause.

Examination revealed: marked pallor of the temporal halves of both disks; diminution of tactile sensation of the mucous membrane in the right nostril; slight lower left facial paralysis, with a suggestion of dissociation between emotional and voluntary movement; hearing diminished on both sides; slight suggestion of atrophy of the upper part of the right trapezius muscle. Otherwise nothing abnormal was found. There was pronounced weakness and marked rigidity of both lower limbs, of the trunk and of the left upper limb; also weakness of the right upper limb. There was marked intension tremor of both upper limbs, more pronounced on the left. The Romberg sign was present. There was no distinct sensory loss. The plantar reflexes, gave extensor response on both sides. All deep reflexes were brisk, more so on the left. Pathologic flexion reflex was present on the left, but not on the right. There was a faint abdominal reflex of the normal type (with deviation of the umbilicus and the linea alba) on the right side. On the left side, the reflex was more of a "retraction reflex" than a deviation reflex; i. e., the reflex was not unilateral

6. In my clinic this reflex is examined as part of the routine examination by pinching the skin on the dorsal surface of the ankle. If this elicits a flexion reflex comprising dorsal movement at the ankle joint, a pathologic flexion reflex is said to be present.

to the extent that is generally the case. The abdominal reflex elicited from the left half of the abdomen was also constantly accompanied by an extension reflex of the homolateral lower limb. The application of cold elicited the reflex just as easily as the stroking with a pin — and the complex reflex response could also be elicited by application of cold to the left hypochondrium.

The case probably was one of cerebrospinal syphilis (the Wassermann reaction was positive both in the blood and in the spinal fluid). The colloidal gold reaction showed discoloration to violet in a dilution of 1:40 and 1:18. The clinical findings were sufficient to prove that there must be a double pyramidal lesion above the cervical region, the left pyramidal tract being more severely affected than the right one. Of the nature of the left abdominal reflex in this case there can probably be as little doubt as in the preceding case; it belongs to the class of "reflexes of spinal automatism."

SUMMARY

1. One must distinguish between the normal cutaneous abdominal reflex, which is chiefly unilateral with more or less marked deviation of the umbilicus and the linea alba and ordinarily elicitable only by stroking, and pathologic abdominal reflexes.

2. These pathologic abdominal reflexes belong to the order of "reflexes of spinal automatism" and are generally associated with these (flexion or extension reflexes of the lower limbs). When, however, the latter are not pronounced, the distinction between the normal and abnormal abdominal reflexes may be difficult, and one must rely on the following points:

3. The pathologic abdominal reflex has a greater tendency than the normal one to bilateral contraction. It is therefore more a "retraction reflex," while the normal one is more a "unilateral deviation reflex."

4. The pathologic abdominal reflex has sometimes a distinctly prolonged period of latency.

5. It is less elective as regards the stimulus required.

The practical importance of the distinction is chiefly in connection with segmental focal diagnosis. When a pathologic abdominal reflex is wrongly deemed to be a normal one (and in the absence of sensory disturbances, the diagnosis of the level of the lesion depends mainly on motor loss, often slight, and reflex findings), such a mistake may lead to the faulty assumption of a low dorsal or lumbar lesion when the lesion really is situated at a much higher level.

While the existence of a normal abdominal reflex depends on the integrity of the corresponding pyramidal fibers (central efferent reflex path), the pathologic abdominal reflexes just described are independent of the pyramidal tract.

A CLINICAL AND EXPERIMENTAL STUDY OF HYPERTHERMIA *

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Abnormally high temperatures occasionally may be encountered in practically any disease characterized by fever. There are a few conditions, however, in which excessive elevations of temperature are more or less constant and in themselves somewhat diagnostic. The outstanding condition in which hyperthermia is the most conspicuous and characteristic symptom is thermic fever or heat stroke. It is also commonly seen in brain and spinal cord injuries, whether traumatic or surgical in origin. Finally, in this connection must be mentioned the authenticated instances of record-breaking temperatures in hysteria. The term hyperthermia is used in this paper, as defined in most medical dictionaries, to mean "an abnormally high temperature," and is thus synonymous with the term hyperpyrexia, which is arbitrarily understood to be any temperature above 105 or 106 F.

My interest in hyperthermia is the result of its occurrence as one of the principal symptoms of a rather characteristic syndrome encountered in some cases of injuries of the head and occasionally following operations on the brain. It has also been noted after injuries to the cervical spinal cord, Gardiner and Pembrey [1] reported twenty-four such cases, nineteen of which showed hyperthermia. This syndrome is encountered with sufficient frequency to have become a distinct clinical entity in surgery of the brain. The condition commonly has its onset within the first twenty-four hours after injury or operation, and is practically always of unfavorable prognostic import. It is characterized by rapid and sudden elevation of temperature, considerable acceleration of both pulse and respiration and progressively deepening coma. Other symptoms may be present, but are not known to be constant or characteristic. Bagley,[2] in a recent study of three cases, found disturbances of muscular power, increase of deep reflexes, low intracranial pressure and spacticity, while Sharpe [3] mentions a falling blood pressure, increased intracranial

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* Read at the Fiftieth Annual Meeting of the American Neurological Association, Philadelphia, June, 1924.

* This paper is published under a grant from the Neurosurgical Department of the University of Pennsylvania.

1. Gardiner and Pembrey: Guy's Hosp. Rep. **66**:87, 1912.

2. Bagley, C.: Extensive Hemorrhagic Extravasation from the Venous System of Galen, with a Clinical Syndrome, Arch. Surg. **7**:237 (Sept.) 1923.

3. Sharpe: Am. J. M. Sc. **165**:405, 1923.

pressure and fundus changes on opththalmoscopic examination. My observations lead me to believe that it is most frequently encountered postoperatively in patients suffering from basal lesions or in those in coma prior to operation. It is seen not infrequently after exploratory operations in patients with subcortical gliomas. The exact cause of this syndrome has not been determined. Because of the profound disturbances of respiration and circulation with the hyperthermia, it has been thought that the causative factor must be exerting its influence on the medulla. For this reason, as well as for lack of a better explanation, the syndrome is frequently referred to as "medullary edema."

With the hope of throwing some light on the etiology of this condition, an investigation, both clinical and experimental, was undertaken. As the temperature disturbance is such a constant and characteristic feature, it was thought that this afforded a good avenue of approach for an attack on the problem. The rise in temperature of so-called "medullary edema" comes suddenly and is progressive, within a few hours reaching 105 to 108 F. by axilla. This hyperthermia is maintained with slight variations to the time of death. The accompanying coma precludes taking the temperature by mouth. As is well recognized, the axillary method is not a reliable guide to the central body temperature, and it is not unlikely that in "medullary edema" the temperature is considerably higher than is usually recorded by axilla. In one patient in whom the temperature was taken simultaneously by rectum and axilla, the rectal temperature registered two degrees higher than the axillary. The administration of enteroclysis to these patients has prevented the collection of a sufficient number of such observations to be of any value.

PHYSIOLOGY OF BODY TEMPERATURE

The maintenance of a constant temperature is dependent on two distinct bodily functions, namely, heat production and heat dissipation. The balance between the two maintains the body at the optimum temperature for the functioning of cellular protoplasm. Within a fixed range, an alteration of one of these functions is normally compensated for by an alteration in the other.

Heat Production or Thermogenesis.—The chemical reactions necessary to maintain the health and functioning of the cells of the body are accompanied by the evolution of heat. Certain reactions, however, are synthetic in nature and require the absorption of heat for their consummation; but this loss of heat is negligible as compared with the heat resulting from the catabolic processes going on constantly in the tissue cells.

The muscles form the great bulk of the body tissues, and the heat of the body is largely dependent on the activity of muscle cells. The heat produced in muscle tissue is the sum of heat derived from three

sources: the metabolic processes required to maintain life of the cells, the tonic contractions responsible for tonus, and the tetanic contractions which result in the muscular movements of the body. The relative importance of these three sources of muscular heat may possibly be evaluated from a consideration of the effect of curare on body temperature. In a warm-blooded animal, curare produces a poikilothermous condition. Curare acting on the myoneural junction produces complete paralysis by abolition of both tonic and tetanic muscular contractions. The lowering of muscle metabolism accompanying the injection of curare is probably the result of the paralysis produced and not the effect of direct action on the muscle cells. The heat produced from the metabolic processes required to maintain the life of muscle cells is insufficient to maintain the body temperature, and therefore is responsible for only a small portion of the total heat production. It is said that the tonicity of muscles results from the expenditure of a minimal amount of energy. Tonicity, therefore, is not responsible for any great amount of heat. This leaves the metabolism accompanying active muscular movements of the body responsible for the major portion of heat production.

While the muscles are generally recognized as being the chief source of heat production, some think that the glandular organs play a considerable rôle in this respect. To corroborate this it is asserted that the liver has the highest temperature in the body. In addition to the muscular and glandular tissues there are other sources of heat production of less importance. Chief among these are the metabolic processes of tissues other than those already mentioned, the absorption of heat from external sources, the heat derived from the ingestion of hot foods and drinks and the heat evolved in the frictional movements of the various tissue on each other.

Heat Dissipation or Thermolysis.—First and foremost of the factors concerned in heat elimination is the conduction and radiation of heat from the body surface. There is also continuous conduction of heat to the clothing in contact with the body. Loss of heat by means of conduction and radiation is thought to comprise approximately 73 per cent. of the total heat loss.[4] The area of the body surface, therefore, is a factor of considerable importance. The greater the surface area as compared with the body weight, the greater does the loss of heat become. Next in importance is the evaporation of moisture from the skin. Heat is also constantly being given off in warming the inspired air and in the moisture of the expired air. The urine and feces, being excreted at body temperature, offer another channel for the loss of body heat. The ingestion of cold foods and drinks takes up a small quantity of heat.

4. Howell: Textbook of Physiology, Philadelphia, W. B. Saunders Company, 1921, p. 960.

Finally, as has been mentioned, certain chemical reactions of the body are accompanied by the absorption rather than the liberation of heat. Disturbance in any of these means of heat elimination will be, to a certain extent, compensated for by those remaining undisturbed. The first two sources, conduction and radiation and the evaporation of moisture from the skin, are by far the most important, and it is only through disturbances of these that any serious derangement of heat dissipation is brought about.

Heat Regulation or Thermotaxis.—That heat regulation is under the direct control of the central nervous system appears fairly well established. In poikilothermous animals, this system is rudimentary, and in warm-blooded animals there is a marked variation in the efficiency of the heat regulating mechanism proportional to the extent to which the nervous system has been evolved. The dependence of temperature regulation on the central nervous system was first called attention to by B. C. Brodie,[5] who reported the case of a man with a forcible separation of the fifth and sixth cervical vertebrae and a temperature between the scrotum and thigh of 111 F. Experimentally, Kennaway and Pembrey [6] found in animals with the spinal cord divided just below the brachial plexus that the anterior portion exhibited warm-blooded and the posterior portion cold-blooded characteristics.

Tscheschichin,[7] in 1866, was apparently the first to proclaim the existence of a heat center somewhere above the medulla. This he designated as a moderator or inhibitory heat center, as transection between the medulla and pons produced a marked elevation in temperature. Later, other observers noted a rise in temperature as a result of experimental injury to the brain. Wood,[8] in 1880, following the lead of Eulenberg and Landois and of Hitzig, found that destruction of the first cerebral convolution in the dog posterior to and in the vicinity of the sulcus cruciatus was followed at once by a decided increase in heat production, while with irritation of the same nervous tract there was a decided decrease. Ott,[9] in 1884, demonstrated an area in the brain with a specific influence on body temperature, and stated that in the vicinity of the corpora striata are centers that have a relation to the temperature of the body; the following year he came to a more definite localization in the anterior inner end of the optic thalamus.[10] Later in the same year, 1885, Aronsohn and Sachs [11] described for the first time the so-called

5. Brodie, B. C.: Med. Chir. Tr., London **20**:146, 1837.
6. Kennaway and Pembrey: J. Physiol. **45**:82, 1912.
7. Tscheschichin: Arch. Physiol. **151**, 1866.
8. Wood, H. C.: Fever, Smithsonian Contribution, Washington, 1880.
9. Ott: J. Nerv. & Ment. Dis. **11**:141 (April) 1884.
10. Ott: Phil. Med. News **47**:6 (July) 1885.
11. Aronsohn and Sachs: Arch. f. d. ges. Physiol. **37**:232, 1885.

heat puncture method by means of which they demonstrated a heat center in the medical aspect of the corpus striatum. Baginsky and Lehman,[12] in 1886, demonstrated that the corpora striata are involved in the regulation of body temperature. Hale White,[13] in 1890, produced hyperthermia in rabbits by puncture of the corpora striata and optic thalami, the former giving the highest elevations of temperature. The following year, the same observer [14] showed that injury to the corpus striatum and septum lucidum caused a rise in temperature and that the lesion need only be unilateral. He found no elevation after injury to the optic thalamus, to the white matter around the optic thalamus and corpus striatum or to the cerebellum. Ito,[15] 1899, confirms the existence of a heat center in the corpus striatum. Aisenstat,[16] 1909, found that the maximum temperature could be obtained in rabbits by puncture of the anteromedial portion of the optic thalamus. There was also a rise from puncture of the nucleus caudatus and corpus striatum. The same conclusions were arrived at the following year by Streerath.[17] In 1911, Nikolaides and Dontas [18] demonstrated centers for heat and heat polypnea in the corpora striata of the dog; Sachs,[19] on the other hand, stated that the optic thalamus, nucleus caudatus and nucleus lenticularis contain no centers that on direct stimulation produce changes in temperature. Jacobj and Roemer,[20] in 1912, by injection of irritants into the ventricles, came to the conclusion that the hyperthermia of heat puncture was the result of distention, irritation and hyperemia of the walls of the lateral ventricles. In the same year, Barbour [21] demonstrated that heating the anterior region of the corpus striatum lowers body temperature, while cooling has the opposite effect. In 1913, Barbour and Wing [22] produced an increase in temperature by the direct application of pyretic substances to the corpus striatum; a lowering resulted from antipyretics. These results were confirmed the following year by Cloetta and Waser,[23] also by Hashimoto.[24] Isenschmidt and Schnitzler,[25] in 1914, stated that the

12. Baginsky and Lehman: Virchow's Arch. f. path. Anat. **106**:258, 1886.
13. White, Hale: J. Physiol. **11**:1, 1890.
14. White, Hale: Brit. M. J. **1**:569 (March) 1891.
15. Ito: Ztschr. f. Biol. **38**:63, 1899.
16. Aisenstat: Arch. f. Anat. u. Physiol., 1909, Phys. Abt. p. 475.
17. Streerath: Arch. f. Anat. u. Physiol., 1910, Phys. Abt. p. 295.
18. Nikolaides and Dontas: Arch. f. Anat. u. Physiol., 1911, Phys. Abt. p. 249.
19. Sachs, E.: J. Exper. Med. **14**:408, 1911.
20. Jacobj and Roemer: Arch. f. Exper. Path. u. Pharmacol. **70**:149, 1912.
21. Barbour: Arch. f. exper. Path. u. Pharmacol. **70**:1, 1912.
22. Barbour and Wing: J. Pharmacol. & Exper. Therap. **5**:105, 1913.
23. Cloetta and Waser: Arch. f. exper. Path. u. Pharmacol. **77**:16, 1914.
24. Hashimoto: Arch. f. exper. Path. u. Pharmacol. **78**:394, 1914.
25. Isenschmidt and Schnitzler: Arch. f. exper. Path. u. Pharmacol. **76**:202, 1914.

tuber cinereum in the rabbit is the most important central organ for heat regulation. Sachs and Green,[26] in 1916, were unable to confirm the existence of a cerebral heat center in the caudate nucleus by the use of various methods giving positive results in the hands of other investigators. Lillian Moore,[27] in 1918, also obtained negative results by puncture and removal of the corpora striata. Rogers,[28] in 1919, demonstrated in decerebrate pigeons that if the optic thalami are cauterized, the animals lose control of temperature. Similar results were obtained in decerebrate cats by Bazett and Penfield [29] in 1922.

While this does not cover all the literature dealing with the so-called cerebral heat center, it points out that various parts of the brain have been demonstrated as being essential to temperature regulation, and the numerous contradictory reports prove that the existence of such a center is far from being incontrovertibly established.

The exact mechanism by means of which the nervous system acts to bring about the variations in temperature found in health and disease is as difficult to explain and certainly as important. Recently, Barbour [30] has attempted to explain it on the basis of the water balance of the body. He has shown that elevations of temperature are accompanied by a fluid concentration of the blood, while a dilution occurs in those conditions in which there is a fall in temperature. Another possibility is that heat regulation may be entirely a function of the nervous system, dependent on hot and cold nerve stimuli produced endogenously and exogenously and resulting reflexly in changes of heat production and dissipation. Or is it possibly a function of body metabolism, the alterations in heat dissipation depending reflexly on oxidative processes? The influence of the temperature of the circulating blood on heat regulation is interesting. MacLeod [31] states that heating the blood in the carotid arteries going to the brain causes a fall in rectal temperature. The effect of toxins on body temperature is indisputable, so that the thought has naturally arisen whether or not all alterations in temperature are not the result of substances circulating in the blood stream. As yet none of these hypotheses has been found adequate to explain all the variations in temperature, normal and abnormal, that are encountered clinically and experimentally.

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26. Sachs and Green: Am. J. Physiol. **42**:603, 1916.
27. Moore, L. M.: Am. J. Physiol. **46**:253, 1918.
28. Rogers, F. T.: Am. J. Physiol. **49**:271, 1919.
29. Bazett and Penfield: Brain **45**:185, 1922.
30. Barbour: Physiol. Rev. **1**:295, 1921.
31. MacLeod: Physiology and Biochemistry, St. Louis, C. V. Mosby Company, 1922, p. 745.

DERANGEMENTS OF BODY TEMPERATURE

Disturbances characterized by overheating of the body are far more frequent than those caused by the opposite condition. It was many years before the reaction that is commonly spoken of as fever came to be recognized as a defensive mechanism, beneficial to the organism. It is only when fever becomes excessive or protracted that it is injurious. This reaction is one of the commonest to which the human body is subject, and is naturally, therefore, produced by a large variety of causes. But regardless of the cause, the question arises as to how the temperature regulating mechanism is affected to produce a rise in body temperature. We may think of the causative factor as acting on any part of this mechanism. An increase in heat production can only come about by an increase in metabolism, which must result either from the food ingested or the utilization of the body tissues. Unless this increase in heat production becomes excessive, the body, under ordinary conditions, is able to maintain a normal temperature by increasing the heat eliminated. When the quantity of heat produced exceeds that which the body is capable of compensating for, there is an accumulation of heat to the point where the excessive temperature causes a breakdown in the regulating mechanism in the brain, the temperature, as a result, mounting still higher until death occurs. Death in this instance is probably the result of the concomitant ill effect of the temperature on the respiratory, circulatory and vasomotor functions. If, on the other hand, the primary disturbance concerns those factors having to do with heat elimination, so that this falls below the normal requirements of the body, there is again an accumulation of heat. The first effect of this rise in temperature is an attempt to increase heat elimination through cutaneous vasodilatation and sweating, but since these are primarily affected, there is no response, with resultant retention of heat, which finally reaches a degree sufficient seriously to affect the vital functions of the brain. Unless relief is obtained this ends in death. Finally, if the primary disturbance is in the brain in those areas apparently essential to this mechanism, the direct result is a vasoconstriction of the cutaneous vessels and a marked diminution in the activity of the sweat glands. If this reaction is brought about suddenly, the rapid cooling of the body surface stimulates the cold nerves of the skin; these impulses are transmitted to the brain, give rise to the sensation of a chill and shivering occurs. In addition, cooling of the skin results reflexly in an increase in muscular metabolism, probably through a stimulation of the cells of the motor area. The shivering and the increased muscular metabolism cause increased production of heat, which must be retained, as the brain has lost its power of regulation. If the disturbance in the brain comes about gradually, the vasomotor reaction in the peripheral circulation is

much less, and the sensation of chill and the shivering are absent. There is, however, the same reflex increase in muscular metabolism, causing a rise in temperature which occurs more gradually and is usually much less in degree. It is extremely doubtful whether a primary increase in heat production alone is ever the cause of fevers encountered clinically. In the well-known example of heat stroke, the primary disturbance is one of heat elimination. But the great majority of fevers are the result of a primary derangement of temperature pathways in the brain.

EXPERIMENTAL DATA

Being impressed with the theory of a cerebral heat center, and thinking that possibly the hyperthermia of "medullary edema" might be the result of a disturbance of such a center, I produced destructive lesions

Type of lesion produced by radium emanations.

in the brain of the dog in the hope of reproducing experimentally the syndrome encountered clinically. The basal ganglia appeared to be the most likely localization of the heat center; consequently, the early experiments were concerned with lesions in this area. Later, however, the pons, medulla and pituitary gland were also investigated. In the first series of experiments, destructive lesions were produced by implanting in the basal ganglia small glass tubes containing radium emanations. These were obtained through the courtesy and cooperation of the Laboratories of the Philadelphia General Hospital. The operative approach was through a trephine opening in the left temporal fossa. Both unilateral and bilateral lesions were produced. As it was not intended that the lesions should be of any definite size, the strength of the radium emanations varied in the different experiments from 0.11 to 0.28 millicuries. A 2 inch, 22 gage hypodermic needle, previously loaded with a glass radium emanation tube, was inserted into the brain

substance in the region desired. The tube was then deposited in the brain by pushing it out of the needle with a wire stylet. The accompanying illustration shows the type of lesion produced by radium emanations. Histologic examination of similar lesions by Dr. G. P. McCouch has shown that the effect of radium is far more widespread than the gross appearance would indicate.

As no marked degree of hyperthermia resulted from these experiments, it was thought that the action of the radium was too slow, thus permitting a compensatory mechanism to manifest itself and prevent any marked disturbance of temperature. I therefore next tried the immediate effect of destructive lesions produced by an electric current. The operative procedure was the same. The electrode used to produce the lesions was of the unipolar type described by Horsley and Clarke.[32] It consisted of a fine glass needle enclosing a metal conductor, only the tip of which projected from the end of the needle, around which destruction of the brain tissue occurred. Iridoplatinum is the metal advised for this needle, but in my experiments various conductors were used in addition, including copper, German silver, silver solder and ordinary platinum wire. Satisfactory lesions were produced with all, but the current strength could not be maintained at a constant level with any needle except those composed of platinum or iridoplatinum. The needle was employed as the anode, while a copper plate attached to a shaved area on the animal's hind leg formed the cathode. The laboratory current of 115 volts direct current was passed through a rheostat used as a potentiometer, and this in conjunction with the resistance encountered in the animal's body gave a current strength that could be maintained at 10 milliamperes. This current was permitted to flow for varying periods of from two to six minutes for a given lesion. The lesions produced by this method were in all respects similar in gross appearance to those resulting from the radium.

The results of this series of experiments, not differing materially from those of the first, caused me to change the location of investigation to the medulla and pons. Here lesions were produced by means of radium emanations. The small glass tubes were implanted in the tissues through a needle as already described, the medulla and pons being reached by the insertion of the needle through the tissues of the back of the neck between the skull and atlas and directed to pass through the foramen magnum; the method is that employed for cisternal puncture. At first an ordinary lumbar puncture needle, 4 inch, 17 gage, was used, but its large size produced such damage to the medulla as to give rise to an undesirable general paralysis. Consequently, a 2 inch, 22 gage needle was used, which did not result in any ill effects.

32. Horsley and Clarke: Brain **31**:45, 1908.

During the course of the work, a number of miscellaneous experiments were performed. In one of these, a lesion was produced by the injection of 2 minims (0.1 c.c.) of chloroform; in another, 5 c.c. of freshly drawn blood from the animal's heart was injected into the basal tissues, and in a third, 2 c.c. of cerebrospinal fluid was injected intravenously. This report also includes four experiments by Dr. J. E. Sweet in which the pituitary gland was destroyed. In two control experiments, small glass tubes not containing radium emanations were implanted in the basal ganglia. In all, thirty experiments were performed.

In order to determine the normal temperature of the animals used, 118 observations were made on twenty-eight dogs. All temperatures were taken by rectum. The readings ranged from 38 to 40 C., with an average of 38.7 C. This is in practical agreement with other observers; for example, Lusk in some of his metabolic studies on dogs gives 38.4 C. as the average normal temperature. The temperature of the dog will vary with the slightest provocation. For example, it was repeatedly noted that removal of a dog from the animal house up several flights of stairs to the laboratory was sufficient to increase the temperature 1 C., and keeping the animal quiet for as short a period as twenty minutes prior to the administration of an anesthetic caused a lowering of temperature of 0.6 C. These facts emphasize the care necessary in interpreting slight degrees of temperature variations in the dog. With the thought that the rectal temperature might not be a true indication of the central body temperature, a series of ten observations on different animals were made, in which a thermometer fastened into the lower end of an ordinary stomach tube was passed into the dog's stomach. The intragastric temperature in these observations coincided within 0.2 F. with the rectal temperature. In the animals in which radium emanations were used temperature observations were made daily, usually in the afternoon, for as long a period as deemed necessary, while in the electrical experiments in which the destruction of tissue was immediate, the temperature was recorded hourly until it became constant or returned to normal. Thereafter the temperature was taken daily. In a number of instances, temperature observations were made daily for several days or weeks prior to the operation.

In seven instances the lesions produced were sufficient to cause death in from one to three days; necropsies were performed on the other animals, with the exception of two pituitary dogs which are still alive, at periods of from five days to five months after operation. At necropsy, lesions were found to involve the following structures: optic thalamus, corpus striatum, corpus callosum, corona radiata, internal capsule, frontal and parietal cortical areas, nucleus amygdalae, pons, medulla and

Summary of Experiments Performed, Lesions Produced and Resultant Temperature

Experiment No.	Nature of Experiment	Time of Necropsy	Location and Extent of Lesion											Temperature Range, Centigrade
			Optic Thalamus	Corpus Striatum	Pons	Medulla	Corpus Callosum	Internal Capsule	Corona Radiata	Cortex	Nucleus Amygdalae	Internal Hydrocephalus	Pituitary Gland	
1	Control	21st day	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	37.8-38.1
2	Control	68th day	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	38.4-38.8
3	Radium, 0.81 millicurie	7th day	Left, extensive	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	37.8-39.4
4	Radium, 0.63 millicurie	31st day	.....	Left, moderate	.....	.....	.....	Left, moderate	.....	.....	.....	.....	.....	39.0-39.8
5	Radium, 0.61 millicurie	42d day	.....	.....	.....	.....	.....	.....	.....	.....	Left, moderate	.....	.....	38.2-39.3
6	Radium, 0.7 millicurie.	159th day	Left, moderate	.....	.....	.....	.....	Left, moderate	.....	Left, moderate	.....	Left, extensive	.....	38.1-39.7
7	Radium, 0.35 millicurie	14th day	.....	.....	Right, moderate	.....	.....	.....	.....	.....	Right, moderate	.....	.....	37.7-39.3
8	Radium, 0.35 millicurie	8th day	.....	Right, moderate	.....	.....	.....	.....	.....	.....	.....	.....	.....	38.2-38.8
9	Radium, 1.22 millicurie	Died 3d day	Bilateral, extensive	Bilateral, moderate	Bilateral, moderate	.....	.....	Bilateral, extensive	.....	.....	.....	Bilateral, extensive	.....	36.2-41.0
10	Radium, 1.04 millicurie	115th day	Bilateral, moderate	.....	.....	.....	Extensive	Left, moderate	Left, moderate	.....	.....	.....	.....	38.0-39.2
11	Radium, 1.19 millicurie	32d day	.....	Bilateral, slight	.....	.....	Extensive	Bilateral, moderate	.....	.....	.....	Bilateral, moderate	.....	37.4-39.3
12	Radium, 1.28 millicurie	Died 2d day	.....	Bilateral, moderate	.....	.....	.....	Bilateral, moderate	.....	Left, moderate	.....	Bilateral, moderate	.....	38.6-40.1
13	Injection of chloroform, 2 minims	80th day	Right, slight	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	38.0-39.3
14	Electric, 10 milliamperes 10 minutes	75th day	.....	Left, slight	.....	.....	Slight	Left, slight	.....	.....	.....	Bilateral, slight	.....	38.5-39.8
15	Electric, 4 lesions, 10 milliamperes 6 min.	Died 3d day	Left, moderate	Left, moderate	.....	.....	Moderate	Left, moderate	Left, moderate	Bilateral, moderate	.....	Bilateral, moderate	.....	39.3-40.1
16	Electric, 2 lesions, 10 milliamperes 6 min.	Died 1st day	.....	Left, moderate	.....	.....	Moderate	.....	Left, moderate	Bilateral, moderate	.....	.....	.....	38.8-40.0
17	Electric, 10 milliamperes 6 minutes	Died 2d day	.....	.....	Bilateral, moderate	Bilateral, moderate	.....	.....	.....	.....	.....	.....	.....	39.2-40.3
18	Radium, 0.11 millicurie	Died 2d day	.....	.....	.....	Bilateral, moderate	.....	.....	.....	.....	.....	.....	.....	36.0-38.8
19	Radium, 0.44 millicurie	8th day	.....	.....	Left, moderate	.....	.....	.....	.....	.....	.....	.....	.....	38.8-40.1
20	Radium, 0.54 millicurie	17th day	.....	.....	Left, slight	.....	.....	.....	.....	.....	.....	.....	.....	37.8-38.6
21	Electric, 5 milliamperes 2 minutes	33d day	.....	.....	.....	Left, slight	.....	.....	.....	.....	.....	.....	.....	38.0-39.6
22	Electric, 2 lesions, 5 milliamperes 5 min.	5th day	Bilateral, moderate	Bilateral, moderate	.....	.....	.....	Left, extensive	Left, extensive	Left, extensive	.....	Bilateral, moderate	.....	37.5-39.2
23	Injection cerebrospinal fluid, 2 c.c.	24th day	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	38.5-39.4
24	Radium, 1 millicurie...	Died 1st day	.....	.....	.....	Left, extensive	.....	.....	.....	.....	.....	Bilateral, moderate	.....	38.7-41.2
25	Injection blood, 5 c.c..	19th day	.....	.....	.....	.....	.....	.....	Left, moderate	Left, extensive	.....	.....	.....	39.1-40.3
26	Radium, 1 millicurie...	19th day	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	38.3-39.4
27	Pituitary, crushed.....	88th day	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Posterior lobe, extensive	38.1-38.8
28	Electric, lesion in pituitary	Still living	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	38.2-39.2
29	Electric, lesion in pituitary	25th day	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	Moderate	37.6-39.3
30	Electric, lesion in pituitary	Still living	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	37.8-39.4

pituitary body. Internal hydrocephalus was found as a frequent accompaniment. The temperature ranged from 36 to 41.2 C. The low temperatures were observed in animals in which a more or less general paralysis resulted. The accompanying table gives a résumé of the experiments performed.

COMMENT

If the term hyperthermia means an abnormally high temperature, the temperatures produced in these experiments do not constitute hyperthermia. From the standpoint, therefore, of reproducing a condition analogous to "medullary edema," these experiments are negative. In only six did the temperature exceed 40 C., that being the highest temperature obtained in the normal observations. If these six experiments are suggestive, it would be interesting to note the outstanding features. Five of the animals died within three days after operation; only two showed involvement of the optic thalamus, three had involvement of the corpus striatum, three of the pons, two of the medulla, and in four there was an associated internal hydrocephalus. The other twenty-four experiments, in which the temperature did not exceed 40 C., differ from these six in that: the general reaction to the lesion produced was not as severe; with two exceptions, the animals did not die as the result of the lesion; for the most part the dosage of radium emanations or the strength of the electric current employed was not as great; with few exceptions, the lesion produced was not as extensive.

From these experiments, therefore, it may be concluded that: the highest temperatures produced were not dependent on a lesion in any special area of the brain; the temperatures were, on the other hand, most likely the result of a general disturbance of the basal ganglia and brain stem, if not of the entire brain; the early death of the animals showing any suggestion of hyperthermia would indicate that the temperature reactions were merely an associated phenomenon, probably dependent on derangement of those vital functions necessary to the maintenance of life.

SUMMARY

From the review of the literature, as well as the conclusions drawn from my own experimental work, I feel that the use of the term heat or temperature center as indicating a definite spot in the brain whose sole function is the regulation of temperature is misleading, and the term should therefore be dropped from physiologic and clinical considerations of temperature regulation. Unquestionably, there are in the brain widely distributed reflex arcs that are essential to the maintenance of body temperature. These arcs find their chief pathways in the basal ganglia and brain stem, and are intimately associated with other vital functions

itary living
29 Electric, lesion in pitu- 25th day Moderate 37.6-39.3
itary
30 Electric, lesion in pitu- Still 37.8-39.4
itary living

of the body, namely, circulatory, vasomotor and respiratory. It is through derangement of these pathways that temperature disturbances are brought about.

From this study I am led to the belief that the hyperthermia of so-called "medullary edema" does not differ essentially in its mechanism from other fevers encountered clinically. The brain is the all important factor in temperature regulation. The excessive elevation of temperature in "medullary edema" is the direct result of a profound and general disturbance of the brain. The exact nature of this disturbance is not definitely known. Bagley [2] has suggested that it is the result of an extensive hemorrhagic extravasation from the venous system of Galen. I am inclined to the belief, however, that all fevers are of toxic origin, whether this be the result of poisons introduced into the body as in infectious diseases, the absorption of toxins from localized areas of tissue destruction or gangrene, as exemplified by sapremia, or the retention of normal or abnormal products of metabolism as seen in gout and uremia. There are several possibilities as to the source of the toxins in brain injuries. Prominent among these are the toxins liberated from sudden and extensive destruction of brain tissue, an alteration in the metabolism of the brain cells giving rise to toxic products, or possibly a disturbance of the function of the choroid plexus which results in the liberation of toxins in the cerebrospinal fluid. With a better understanding of the mechanism of temperature regulation in general will come the solution of the problem of hyperthermia in so-called "medullary edema." Just what bearing the solution of this problem will have on clinical practice is at present not entirely clear, but it is manifest that this solution constitutes the first step toward an understanding of a condition which is of vital importance to the proper management of patients suffering from intracranial lesions.

CONCLUSIONS

1. In only six of a series of thirty experiments in which destructive lesions were produced in the brain of the dog did the temperature exceed that normally observed in this animal.

2. By means of such lesions, a condition simulating so-called "medullary edema" did not result.

3. The hyperthermia of "medullary edema" is not dependent on a lesion in any definite area of the brain, but is rather the result of a disturbance of widely distributed reflex arcs essential to the maintenance of body temperature.

4. The existence of a cerebral heat center is not confirmed.

Clinical and Occasional Notes

THE LIPIODOL TEST FOR PATENCY OF THE CEREBRO-SPINAL CANAL IN A CASE OF SCIATICA (?) WITH UNUSUAL FEATURES

NORMAN VINER, M.D., MONTREAL, CANADA

History.—On July 25, 1924, Mrs. W. L., aged 35, came to the Western Hospital, complaining of inability to sit or walk on account of severe pain across the lower part of the back and down the right leg. In May, 1923, she had pain across the middle of the back. She received massage for two weeks, and her condition improved. The following August, she went swimming, and the pain returned. She was then sent to a hospital, with a diagnosis of lumbago and sciatica. She stayed there for six weeks, returned home unimproved and remained in bed until after January 1, when she made some effort to walk. For a few days, she was able to get to the front door and back once daily, but she found the strain too great, so ceased to try. It was during these efforts that she noticed that the toes of the right foot tended to drop. Pain was excessive when she tried to walk or sit, especially with the legs hanging down. A sharp shooting pain extended all the way down the back of the thigh and leg to the dorsum of the foot, and it remained as a dull ache for about fifteen minutes after she resumed the recumbent position. Lying on the right side would start the pain. There was no subjective numbness or change to heat or cold. She never suffered from headache, and vomiting occurred only on admission to the hospital, apparently due to some gastric disturbance. There was no history of venereal disease or of anything suggestive of any other neurologic lesion. She had suffered from rheumatism at the age of 15 and typhoid at the age of 19. She was otherwise healthy and athletic. She had two children; in both cases, the delivery was instrumental. One of the children suffered from infantile paralysis and had to wear a brace.

Examination.—Through the courtesy of Drs. Robbins and Kerr, I made an examination on July 15, 1924. The patient was a rather plump woman, of normal intelligence and bearing and of cheerful temperament. The results of general examination were negative. There was great pain over the right gluteal region, extending along the back of the thigh and leg to the front of the leg and dorsum of the foot, whenever the patient stood or sat. There was slight diminution in sensation to cotton and pin prick over the shin and outer side of the dorsum of the foot to the roots of the first and second toes (fifth lumbar). There was marked tenderness to pressure at the point of exit of the sciatic and, to a less degree, along the back of the thigh. Lasèque's sign was present. A modification of this test, which I think reliable, was markedly positive. This test consists in raising the whole limb, with the knee extended, to as near a right angle with the body as possible. The foot is then at right angles to the leg. The leg is then steadied with one hand, while the other sharply dorsiflexes the foot. In involvement of the sciatic, this movement is painful. The movements of the limb were normal, any limitation present being due to pain and not to weakness. There was little, if any, wasting. Sense of position of the toes and of the other joints was normal. The reflexes elsewhere, as well as all other findings, were normal; in the affected leg, however, the knee reflex was almost absent, and the Achilles reflex was doubtful. There was, however, a definite right Babinski sign, which apparently removed all justifica-

tion for calling the condition sciatica or sciatic neuritis. On the other hand, all efforts to confirm the Babinski sign by ankle or rectus clonus, by a MacCarthy, Gordon, Oppenheim, Chaddock or Mendel-Bechterew reflex were unsuccessful. I then thought to discredit the Babinski sign in view of the fact that the patient's ability to flex the right toe voluntarily, although present, was greatly diminished as compared with the left one. Whether or not this attitude was justified remains to be established; at any rate, it was unsatisfactory. It might be added by way of parenthesis that with frequent efforts on the patient's part this voluntary flexion increased to a visible degree but

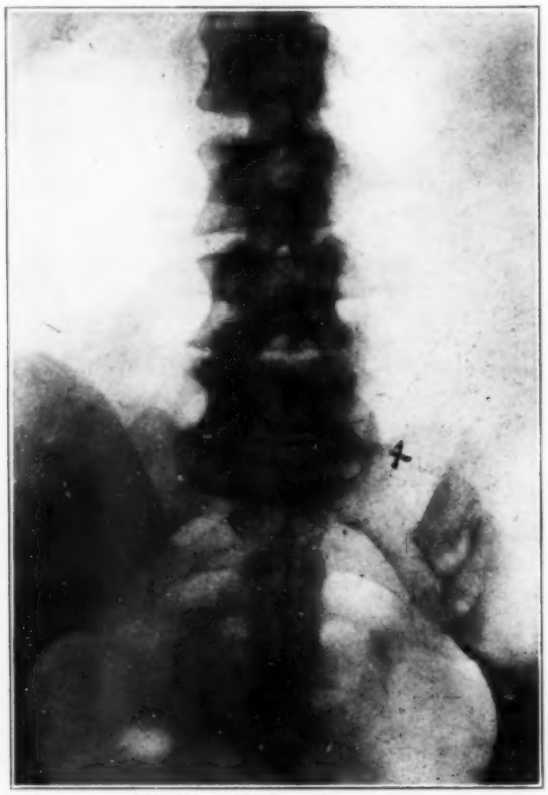

Fig. 1.—Squat appearance at ×.

without affecting the Babinski sign. Simultaneous puncture in the second and fifth lumbar spaces by Dr. Mackay early in July, 1924, had shown no xanthochromia, no bacteria, practically no globulin, a negative Wassermann reaction and only 6 cells per cubic millimeter in each specimen. A number of roentgenograms of the lower spine and pelvis, taken by Dr. Ross, indicated a rather squatty appearance at the sacrovertebral angle (Fig. 1, *x*) but the deviation from normal was not considered remarkable.

Treatment and Course.—As the Babinski sign persisted, late in July it was decided that an effort should be made to determine whether there was a

block in the cerebrospinal canal. There was a choice of two methods: Ayer's [1] combined cistern and lumbar puncture, with which I have had some experience, or Sicard's [2] method of injecting from 1 to 2 c.c. of lipiodol (Lafay) into the cisterna magna with the patient in a sedentary or semirecumbent position. This preparation is impervious to the roentgen rays and sinks down in the cerebrospinal canal by gravity, until it encounters an obstruction which it thus demarcates. Ayer's method is open to the objection that when it diagnoses an obstruction, it fails to localize it; second, one cannot insert a needle as low as the lipiodol will sink in a patent spinal canal.[3] Thousands of successful cases by Ayer's method [4] have been reported. On the other hand, every recent volume of *La Revue Neurologique* or *La Presse Médicale* has reported several good results by Sicard's method. Sargent [5] and others in England have given some equally satisfactory reports. Finally, Russel [6] in America

Fig. 2.—Residual lipiodol in tissues of neck.

1. Ayer, James B.: Spinal Subarachnoid Block as Determined by Combined Cistern and Lumbar Puncture, Arch. Neurol. & Psychiat. **7**:38 (Jan.) 1922.

2. Sicard, J. A.; Paraf, P., and Laplane, L.: Spinal Radiography by Means of Lipiodol, Presse méd. **31**:885 (Oct. 24) 1923.

3. One must, however, admit that Ayer has an excellent alternative method in cases of block low down in the spinal canal—the combined lumbar and sacral-epidural puncture. Cushing, Harvey and Ayer: Xanthochromia and Increased Protein in Spinal Fluid Above Tumors of the Cauda Equina, Arch. Neurol. & Psychiat. **10**:167 (Aug.) 1923.

4. Ayer, James B.: Puncture of the Cisterna Magna, J. A. M. A. **81**:358 (Aug. 4) 1923.

5. Sargent, Percy: Radiographic Localization of Spinal Lesions by Sicard's Method, Brit. M. J. No. 3266, 174 (Aug. 4) 1923.

6. Russel, Ethel C.: Localization of Spinal Block by Means of Iodized Oil, J. A. M. A. **82**:1775 (May) 1924.

has reported a successful case. The unfavorable criticism of Ayer and Mixter[7] (and Bailey) was based mainly on their experiments on cats, and apparently not on the particular preparation recommended by Sicard. The latter used a preparation consisting of 0.54 cg. of iodin in poppy-seed oil to 1 c.c., whereas the Boston observers used iodipin, which consists of 10 or 25 per cent. of iodin in oil of sesame. This may be stretching a point, but is it beyond the bounds of possibility that the offense lay in the vehicle rather than in the iodin; in other words, that oil of sesame is more irritating in the spinal canal

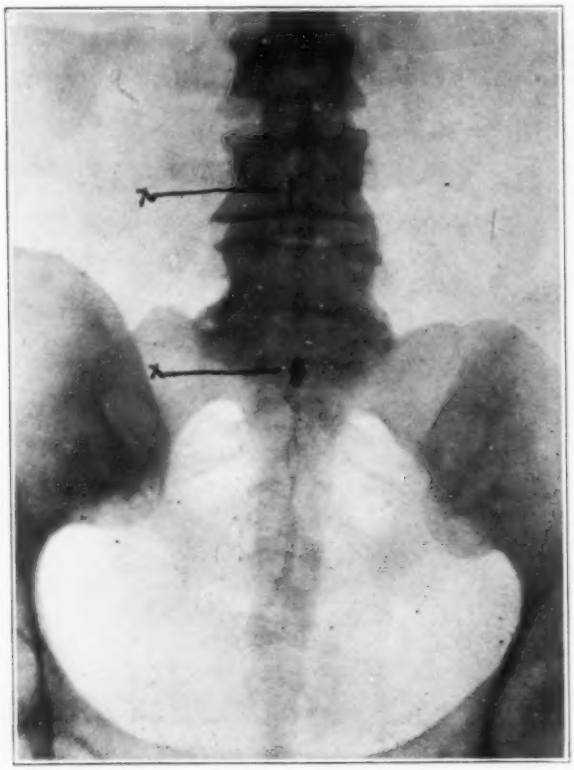

Fig. 3.—Lipiodol descended into sacral canal.

than poppy-seed oil? A rather more important stricture is that of Vincent,[8] who refers to cases of misleading results obtained by Sicard's method.

At any rate, the Sicard method was chosen and on account of the plumpness of the patient, the needle, which had a rubber guard, at 6 c.c. had to be forced beyond this depth. A few drops of cerebrospinal fluid were allowed to drop out, and then the flow ceased. An effort to get in a little deeper elicited from the patient the cry, "Oh doctor, I have the same pain in my good leg." It was therefore deemed advisable to leave the needle in situ,

7. Ayer and Mixter: Proc. Boston Soc. Neurol. & Psychiat., Dec. 6, 1923; Arch. Neurol. & Psychiat. **11**:499 (April) 1924.

8. Vincent, C.: Presse méd. **32**:121 (Feb. 9) 1924.

taking a chance that the lipiodol was getting into the spinal canal. About 1.5 c.c. were injected, of which, as seen in Figure 2, a considerable quantity remained in the tissues of the neck. It is calculated that about 0.5 c.c. got into the cerebrospinal canal, and this, as seen in Figure 3, met with no obstruction, striking the bottom, or approximately, of the cerebrospinal canal. There were no ill effects observed from the lipiodol in the canal; the residual portion, in the tissues of the neck, caused some stiffness and pain in that region, which lasted for about twenty-four hours and was not severe.

The findings here, being negative, it was decided to treat the condition as one of intractable sciatica, or as root pain. In the course of the first half of August, 1924, the patient was given four sacral epidural injections. (Here, too, some difficulty was encountered owing to the patient's stoutness.) Each injection consisted of 20 c.c. of 1 per cent. procain, followed by 80 c.c. of physiologic sodium chlorid. Before the second injection, the patient began to visit other patients in the ward, and the Babinski sign had markedly diminished. The day after the fourth injection, the patient could sit in comfort, lie in any position and walk around the ward. Two or three days later, she was discharged.

On Sept. 13, 1924, she reported progressive improvement in movement with diminution of pain but has had a more or less constant dull ache across the lower part of the back, feels as though her leg were weak, and finds considerable difficulty in mounting stairs. On the other hand, she has been up and about the house a great deal every day, and twice has been out for a walk on the street. As she had been completely bedridden for exactly a year, suffering greatly at the same time, she is delighted with her present state. The physical examination disclosed nothing new. The Babinski sign was still absent, the Achilles reflex was absent, the knee reflex was much diminished, and there was slight diminution of touch and pain as described above.

133 Bishop Street.

News and Comment

ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR THE STUDY OF THE FEEBLEMINDED

The Forty-Ninth Annual Session of the American Association for the Study of the Feebleminded will be held at Raleigh, N. C., May 8, 9, 10 and 11, 1925, at the Hotel Sir Walter. The lengthy program is divided into a number of symposiums as follows:

1. Delinquency and Crime as Related to Mental Deficiency.
2. Psychology and Mental Deficiency.
3. Relation of Mental Deficiency to the Public.
4. Motivation of Special Class Work.
5. The Institution for the Mentally Deficient in Relation to Other Institutions and Agencies.

Abstracts from Current Literature

MULTIPLE SCLEROSIS. GEORGES GUILLAIN, Rev. Neurol. **31**:648 (June) 1924.

This is the second of two addresses delivered before the International meeting under the auspices of the Society of Neurology of Paris, May 30-31, 1924. Guillain refers to the generally accepted anatomoclinical description of the disease as described by Cruveilhier, Charcot and Vulpian; but, like Veraguth, who preceded him, he rejects the so-called "clinical triad" of Charcot, except as existing in a few cases. He gives the plan of his paper as covering the following subjects: the forms of the disease as usually encountered; the diagnostic value of the study of the spinal fluid by the benzoin-colloidal test (a personal study), and recent interesting studies relative to the spirochetal origin of the disorder. He frankly states that the purpose of his paper is not so much to state any certain number of positive conclusions as it is to encourage a discussion of what are still controversial questions.

The Clinical Approach.—Without qualification, he asserts that next to syphilis multiple sclerosis is the most frequent of all diseases of the central nervous system. First, the disease is not often seen until after the third or fourth significant manifestation of some sort or other, and it is not diagnosed usually until one or more years after the actual onset. In his own experience and that of his intern, the condition usually is diagnosed in the second year.

Basing his opinion on the study of patients who are intelligent and observing, he believes the following are some of the earliest diagnostic signs: weakness in walking, intermittent medullary claudication (or symptoms akin to it), slight incoordination of station at the beginning of walking, numbness and tingling of the extremities, blindness or diplopia sudden and transitory, slight ataxia in the upper extremities noticeable in attempts at writing, and slowness in the beginning of micturition. Acute severe outbursts, such as hemiplegia or paraplegia, are rare. As opposed to this, the first symptoms are so fleeting and variable that the patients are often regarded as being neuropathic or hysterical.

Then follows an analytic and critical study of the clinical symptoms. Motor symptoms are mentioned first, and include chiefly: deficiency of motor phenomena, modification of tonus, and disturbances of coordination. Fatigability is one of the first signs. All degrees of spastic paraplegia may be present, but rarely as intense as in medullary compression (such as that due to cord tumor). Weakness of the abdominal muscles may be demonstrated at times by requesting the patient to seat himself without the aid of his arms. Atrophy of the upper or lower extremities without reaction of degeneration may occur, and may simulate amyotrophic lateral sclerosis. Tremor of the intentional type is present in varying frequency. The author says it was present in only 14 per cent. of his own cases. Dysmetria and asynergia appear at times in the upper extremities, as well as adiadokokinesis. Scanning speech, which may be regarded as a form of intention tremor, possibly of cerebellar asynergy and associated with modifications of bulbo-ponto-cerebellar tonus, is also infrequent.

Reflex Disturbances.—In addition to the well recognized increase in the deep tendon reflexes, the author speaks of a clonus, so to speak, of the muscles of the thigh, not described elsewhere to his knowledge, produced by requesting

the patient to flex the thigh on the abdomen, keeping the great toe on the plane of the bed. The result is a rhythmic adduction and abduction of the knees so marked as to cause them to knock against each other. Another example of an associated reflex is that obtained by percussion over the stylo-radial region. This produces contraction in the pectoralis major. Still another is the so-called "medio-pubic reflex." If the symphysis pubis is struck in the normal person, there is a response in the muscles of the abdominal wall above and in those of the thigh, below. In about 50 per cent. of cases of multiple sclerosis, there is either an absence of the upper or the lower response together with the loss of the abdominal reflex.

Considerable value is placed on the cutaneous plantar reflex. The examiner may also obtain a distinct extension of the great toe by stimulating the skin in the areas supplied by the fifth lumbar nerve, and the first and second sacral, i. e., the postero-external aspect of the leg and the posterior aspect of the thigh. Loss of the cutaneous abdominal reflex is present in a very high percentage of cases.

The so-called "reflexes of defense" or "medullary automatism" appears in a number of cases of multiple sclerosis, but is decidedly less frequent than in cases of cord compression. Babinski's favorite method of eliciting the reflex of defense is by pinching the skin of the dorsum of the foot.

Guillain's intern observed that there was a loss of the soft palate reflex (sometimes incorrectly styled "anesthesia of the soft palate") in nineteen out of twenty-four cases. The author believes that this sign is very valuable, that it deserves greater recognition, and that it is almost as important as the loss of the cutaneous abdominal reflex.

Sensory Disturbances.—These include paresthesias, especially in the hands and feet, all of which are as important as ocular disturbances or hyperactivity of the reflexes with fatigability. Often these paresthesias are painful in character, some patients experiencing lacinating or lightning pains. In a few instances, there is itching without any objective cutaneous lesion. While disturbances in the sense of touch, pain, and heat or cold are relatively rare, those of bony sensibility are frequent, especially over the ilium; yet the vibratory sense over the ribs, sternum and the upper extremities remains normal. Astereognosis mentioned by certain authors is rare.

Urinary and Genital Disturbances.—Urinary disturbances were noted as early as the time of Charcot, and have been reported by many later writers. At the beginning of the disease the patients often complain of difficulties in micturition, particularly in starting the stream. These difficulties may be present without any spastic paraplegia. Marquezy has noted imperative and frequent micturition in 40 per cent. of his cases. This does not usually occur early in the disease but rather in the course of its development. In his cases, it takes about two years for these signs to develop. Genital disturbances are rare. Potency is preserved for a long time. The so-called "sacral" form described by Oppenheim and others appears to be exceptional.

Ocular Disturbances.—These have been recognized for a long time. Parinaud insisted on the paralysis of associated movements of the eyeballs and on the importance of myosis coexistent with an exaggeration of the pupillary reflex. Uthoff drew attention to transitory and partial paralyses of the motor apparatus of the eye. Ophthalmologists have frequently called attention to the pallor of the disk, either total or only in a temporal segment, but they have insisted on the importance of this pallor especially in connection with the rarity of the loss

of vision. They have also described alterations of the visual fields. Such visual disturbances are often unilateral.

Cochlear and Vestibular Disturbances.—Certain writers have noted transient deafness at the beginning of the disease which might be compared with transient blindness. Teuffert has found in all cases at the Salpêtrière an intact cochlea. Vertigo is one of the most constant early symptoms of multiple sclerosis, and reappears often in every relapse. It is a gyratory vertigo not usually accompanied by tinnitus, nausea or vomiting, and it is often of short duration and is frequently caused by quick movements of the head. In most of the patients, spontaneous nystagmus exists without vertigo. It has been asserted that static and horizontal nystagmus is absent in patients with intense vertigo, but Marquézy has not been able to establish this.

Nystagmus is one of the most common signs of multiple sclerosis, and, according to various investigators, is present in 50 to 70 per cent. of cases. Lateral nystagmus is the most common form, although rotary may occur. Retrobulbar optic neuritis occurs in a great number of cases and is of great diagnostic importance. Lagrange and Marquézy, by a methodical study of visual disturbances in cases in which there was a negative Wassermann reaction of the blood and spinal fluid and a positive colloidal benzoin reaction, have been able to eliminate all doubtful cases of syphilis and have reached a diagnosis of multiple sclerosis. The author gives percentages of transient diplopia and amblyopia. The conclusions relative to associated paralyses do not conform to the findings of Uthoff and Parinaud. The Argyll Robertson pupil is always absent.

The author believes there is some importance (he and his collaborators give 54 per cent.) in the fact that the pupils do not hold well in their contraction to light; the pupil first contracts promptly and then very soon dilates.

Lagrange, Marquézy and others find a fair number of instances of partial atrophy of the fundus, usually in the lower portion of the temporal segment and most often triangular in shape, the base of the triangle appearing at the margin of the disk.

The writer then refers to experimental examinations of the labyrinth; the caloric and Bárány tests give such different results that no exact conclusions can be drawn, but in most instances various phases of these tests show normal reactions. In the rotary test made on sixteen patients, different results have also been obtained, the nystagmus in some being of shorter duration and in others of longer duration than normal.

The galvanic test of Babinski is shown in one of the author's patients in movement of the head toward the positive pole. Berré believes that labyrinthine disturbances are more important than cerebellar. Signs of hyperexcitability of the labyrinthine pathways exist incontestibly in a number of cases of multiple sclerosis, and, according to Berré, merit serious consideration. According to the author, it is difficult to differentiate midbrain lesions and those in the cerebellar conducting pathways from the physiopathologic symptoms of multiple sclerosis.

Mental Symptoms.—While there is some reference made to euphoria and apathy or depression as characteristic in certain cases and even sometimes states of stupor (syphilis must be ruled out), the author thinks there is no mental state characteristic of multiple sclerosis. He cites in corroboration of his views the opinion of the American Association for Research in Nervous and Mental Diseases held in New York in 1921.

Sympathetic Disorders.—The visceral sympathetic system, vasomotor disturbances of the extremities, the pilomotor reflex, the oculocardiac reflex and arterial pressure, together with disturbances of the internal glands, seem to play little or no part in multiple sclerosis.

Bulbar Symptoms.—These are too well described in classic works to call for enumeration here.

From the discussion of the clinical aspects of multiple sclerosis, their various manifestations, the author passes on to a presentation of studies on the spinal fluid and particularly of the diagnostic value of colloidal reactions. He takes an opposite view from that usually expressed by the most recent French and other foreign neurologists who are inclined to think that the spinal fluid is either normal or only slightly modified in multiple sclerosis. He believes that a study of the spinal fluid gives important information for the early diagnosis of the disease and for the diagnosis of many abortive forms. Exhaustive citations of various authors are given relative to lymphocytosis, hyperalbuminosis, the colloidal gold reaction and the mastic reaction. Reactive to these studies there is a wide difference of opinion. The author then takes up his own studies begun in 1920 in collaboration with others on the benzoin colloidal reaction which, he thinks, with other colloidal reactions, has advantages because of its extreme simplicity, the ease of reading the reactions and the constancy of the conclusions. Shortly after this first work, he noted in a case of multiple sclerosis a slightly positive benzoin reaction in which the Wassermann reaction was negative. He then cites numerous instances in cases reported by others in which the benzoin reaction was positive or subpositive, with a negative Wassermann reaction. Fourteen investigations in the years between 1922 and 1924 are cited.

He notes the following conclusions based on a study of twenty-seven cases in collaboration with Marquézy: a slight increase in pressure of the cerebrospinal fluid (of diagnostic value in attempting to differentiate multiple sclerosis from tumors of the cerebellopontile angle); lymphocytosis generally lacking (usually under 10 lymphocytes to the cubic millimeter); quantitative albumin usually normal, but with a few instances of a slight hyperalbuminosis. There seems to be no relationship existing between this slight hyperalbuminosis and the number of cells. The Pandy reaction is sometimes subpositive, but in most instances it is negative. Increase in globulin is exceptional.

The Wassermann reaction, without a single exception, has proved negative in all the author's cases. Commenting on the value of the benzoin colloidal findings, he usually uses sixteen tubes, regarding that number as indispensable for recognition of the development of the curve of precipitation in the high dilutions and for purposes of judging the eventual modifications of the intensity of the reaction in the course of the evolution of the disease, or of the influence of therapeutic measures.

He finds the benzoin colloidal reaction positive or slightly positive in 63 per cent. of cases. This percentage agrees with the findings of other investigators. The so-called "paralytic" curve is rare. A characteristic curve runs as follows: 00100, 01200, 01100. The author and his intern note a fact not described by others, namely, that the benzoin reaction shows a curve with precipitation toward the right. In their experience, they have not observed precipitation in normal spinal fluid as far as the ninth tube, whereas in multiple sclerosis precipitation in the ninth and tenth tube is almost always constant, this precipitation taking on a real value when the reaction is negative in the first five tubes. When this peculiarity is taken into account even 63 per

cent. is a low estimate for abnormal curves suggestive of multiple sclerosis. This fact, together with a negative Wassermann reaction as compared with a positive Wassermann in syphilis, together with positive findings in syphilitic cases such as increased cell count, increased albumin, a positive Pandy test and the like, make the differentiation between the two diseases much more definite. The author believes that his studies, together with those of other French and foreign investigators, make the benzoin colloidal reaction one of real diagnostic value. Modifications of the spinal fluid in multiple sclerosis might be schematized as follows: Absence of cell increase or slight cell increase, absence of albumin increase or slight albumin increase, negative globulin, and Wassermann tests, a positive or slightly positive benzoin or colloidal gold reaction. In epidemic encephalitis in which the reaction of the colloidal gold is often positive, along with the positive Wassermann reaction, the benzoin colloidal reaction is always negative. These serologic findings so pronounced in multiple sclerosis have proved of great value in the diagnosis of this disease when its first stages are so varied and so difficult to recognize with accuracy.

The "Common Form."—The writer then devotes a section to clinical forms of multiple sclerosis. He thinks there are only a few forms which merit special description. Among the many symptoms, the following are probably the most important early symptoms: incidence between the twentieth and thirtieth year, first signs not easily recognized — including slight and transitory disturbances of gait, paresthesias and vertigo; some months later, a sharp relapse in which the patient complains of fatigability, difficulty in walking, uncertainty of equilibrium, stiffness in the lower extremities, numbness, tingling and difficulty at the beginning of micturition. To these signs are frequently added vertigo, diplopia and diminution of the acuteness of vision and all the long list of other symptoms referred to before, including intention tremor, clonus, double Babinski sign, loss of abdominal reflexes, nystagmus, a negative Wassermann test and positive colloidal reactions.

Frequently many of these symptoms disappear, when the patient may be, on the other hand, unable to walk; then after a number of weeks of rest, there may be remission with normal equilibrium and even the ability to resume former occupations; but in one, two or three years, the same cycle repeats itself, and spastic paraplegia may develop. In this so-called "common form," even after a long period of years, scanning speech and intention tremor may be absent.

The So-Called "Classic" Form.—This form is exceptional, having besides numerous other symptoms the so-called "triad of Charcot." Various writers estimate that it does not occur in more than 10 to 15 per cent. of cases.

The So-Called "Ocular" Type.—This clinical form is one of the most interesting and most important to recognize. The patients show a progressive and rapid diminution of vision and sometimes a sudden unilateral or bilateral blindness, with all signs of a retrobulbar neuritis. The author states that in one of his cases it was not until twenty-two years after the retrobulbar neuritis that the other clinical signs of multiple sclerosis appeared. Sometimes when the ocular signs are the only ones apparent, a methodical examination may disclose overactive tendon reflexes and a loss of the cutaneous abdominal reflexes. The latter signs then have a real value. The author also believes that a study of the spinal fluid at this time would reveal positive colloidal reactions. Various writers report that the usual signs of the disease frequently do not appear until eight, ten, twelve or fourteen years after the retrobulbar neuritis.

The author believes that the existence of retrobulbar neuritis which is not syphilitic in origin or toxic (alcohol or tobacco) may frequently turn out to be multiple sclerosis. He thinks too much emphasis has been laid on infections of the sphenoidal sinus, and that multiple sclerosis is thus overlooked. A complete examination of the nervous system is necessary to avoid falling into this error. It should be supplemented by the colloidal reaction of the spinal fluid. On the other hand, it is necessary to be cautious in giving a prognosis, because retrobulbar neuritis is frequently not a manifestation of multiple sclerosis.

Lagrange and Marquézy, in their study of ocular lesions in multiple sclerosis at the Salpêtrière have come to the same conclusion as the author. An optic neuritis characterized by pallor of the temporal half of the disk, interpreted from a functional point of view as an alteration of the chromatic sense; a central scotoma or a concentric narrowing of the visual field, frequently unilateral and often preceded by a sudden appearance of a transient amblyopia, is undoubtedly a clinical picture which frequently reveals a definite multiple sclerosis.

Pure "Paraplegic" Form.—This form has all the appearances of Erb's spastic paraplegia. The latter has too often been confused with multiple sclerosis. Moreover, Erb's spastic paraplegia has too often been regarded as syphilitic in origin. A spastic paraplegia with lost cutaneous abdominal reflexes and a spinal fluid showing no cells, a normal albumin content, a negative Wassermann reaction, and a positive colloidal gold or benzoin colloidal reaction, may almost with certainty be regarded as a case of multiple sclerosis. Charcot, in the latter part of his life, described certain atypical forms of multiple sclerosis and insisted on one clinical form represented by spastic paraplegia. The later tendency to include all cases of spastic paraplegia in the category of syphilis is extreme and must be reversed in the light of modern biologic investigation.

The Course of the Disease.—In the course of multiple sclerosis, there may be periods when such serious symptoms as blindness, disturbance of gait and spasticity may clear up sufficiently to permit the patient to resume his occupation. This is the reason why patients are frequently regarded as suffering from functional nervous disorders. Sometimes the disease seems to become stationary. Carcot and Pierre Marie have cited cases. In spite of these remissions of variable duration, the infective agent persists in its nervous centers and relapses occur. Such may happen without any special cause, but may be due to fatigue, traumatism, an intercurrent infectious disease or pregnancy. At every relapse, the old signs are accentuated and new symptoms appear.

The duration of the disease is variable, averaging from five to twenty years; cases have been cited as covering a period of thirty or forty years. In patients with paraplegia, confined to bed, death may be due to pulmonary tuberculosis, pneumonia, cystitis, decubitus, or other terminal causes. Death following hemiplegia is rare. Vulpian and Babinski have noted end stages with the syndrome of acute myelitis. An acute transverse myelitis has more than once followed a lumbar puncture, and even more diffuse destruction of the cord has been reported. Marquézy, in a patient who died eight years after the beginning of his disease, noted a terminal period in which there was a change from contracture in extension of the lower extremities to contracture of flexion, this change occurring two months before the patient's death. Vulpian and Déjerine have cited similar cases.

Anatomopathologic Considerations; Sclerotic Patches.—It is not the writer's purpose to discuss facts already established by laboratory observation, but rather to emphasize the exactness of modern technic. In necropsies, there had occasionally been established the existence of thickening and infiltration of the pia mater and of the arachnoid; nevertheless, the characteristic lesions are those of multiple sclerosis. The sclerotic patches have their beginning in a degenerative process often diffuse. The author thinks the attempt to prove a correlation between the clinical symptomatology and these sclerotic patches is misleading. In the topography of the islands of sclerosis, the zones of election are noted: (1) perivascular spaces, (2) subpial zones of the cortex, (3) subependymal gray substance next to the ventricles. The demyelinization of this region is often so intense and so diffuse that the ependyma is almost surrounded by a wide ribbon of tissue deprived of its myelin, 1 to 5 mm. in thickness, extending almost to the walls of the ventricles. Two types of patches are noted: old and new. The old patches of two to three years' duration are in the majority. The axis cylinders are deprived of their myelin and lipoid products, free or included in the carrying elements, and are made up of a fibroneurogliar tissue where the axis cylinders cross. The axis cylinders undergo a great numerical reduction. These lesions of the axis cylinders in the territory of the old sclerotic patches are very much attenuated and seem to have undergone an anatomic restoration. There is not found here the thickening, the vacuolizations, the pseudodegenerative aspects which have been established at the periphery of the patches and outside of them. The vessels do not present any sign of perivascularity, and their lymphatic spaces are completely deprived of degenerative lipoid débris. Patches of recent formation are full of lipoid débris where phagocytosis is produced by the myelophages and the myeloclasts and a phagocytosis of cells of various types. It is important to know that the sclerotic patch is only a relatively larger morphologic entity where every nerve fiber undergoes a different evolution. The degenerative history of every fiber is absolutely independent of the evolution of neighboring fibers. The myelin sheath is invaded by numerous myelophages and myeloclasts. A patch of recent formation is completely surrounded by degenerative products strongly reducing osmic acid. Processes of degeneration in multiple sclerosis occur almost exclusively in cells of neurogliar origin, but the cells of mesodermic origin play an equally important rôle and determine the perivascularity of the plasmolymphocytic form. This disintegration is well described in a recent work of Ivan Bertrand.

Lesions of Nervous Tissue Outside of the Sclerotic Patches.—The author's most interesting remarks on this point are in the concluding paragraph, where he discusses the theories of certain authors on the syphilitic origin of multiple sclerosis, which, he states, is maintained on a fragile anatomopathologic basis. The only argument they offer is the existence of perivascularities on a plasmolymphocytic formula. This type of vascularity is an end reaction which one observes in all processes of rapid disintegration, and which indicates only the contribution of a mesodermic factor destined to supply the glia phagocytes. A perivascularity does not authorize one to assert anything more than the presence of some kind of microbe. Only biologic investigations can warrant drawing conclusions relative to pathology in questions of this character.

Etiologic Factors in Multiple Sclerosis.—The author in his conclusion states that what we do not know as to the etiology of multiple sclerosis is as important as what we do know, and that is very little. He discusses the frequency of the disease at different decades of life, appearing to accept con-

clusions reached by the American Association for Research in Nervous and Mental Diseases, and he quotes rather freely from them. He mentions certain cases in persons past 40 years of age confirmed by necropsy, and one as early as the ninth year, also confirmed by necropsy. As to occupation, he thinks that it has little bearing on the condition, and he does not accept the theory cited by others of the disease being frequent in the rural population. He agrees with Wechsler of New York.

Geographic Distribution.—Here again he accepts the American conclusions that the disease is more common in Europe than in America, that it is exceptional in Japan, and that the black races are less susceptible than the white. In Europe, it is more frequent in the north than in the Mediterranean countries. In Alsace, cases are numerous. In the United States, the majority of cases have been observed in the states of Michigan, Minnesota and Wisconsin, all of these states being adjacent to the Great Lakes.

Everything from congenital malformation down to cold, heat, traumatism and overwork have been expounded as causes of this disease, and generally dismissed. Pierre Marie, as early as 1884, described the disease as growing out of other infectious diseases, such as typhoid, scarlet fever, puerperal infections and the like. This conception has been criticized by many authors. The more recent writers have been unable to discover in many cases any antecedent history, either in the ancestry or in the patients themselves, of infectious diseases that might give rise to multiple sclerosis. Within the last few years, many have been led to believe that we are dealing with a specific infectious malady as specific in its origin as rabies, epidemic encephalitis or syphilis. A number of research workers have thought that the specific agent was a particular spirochete. Before presenting a critical study of works published on the spirochete in multiple sclerosis, the author discusses the relationship of multiple sclerosis to syphilis, epidemic encephalitis and acute ataxia.

Relation to Syphilis.—While there are certain symptoms common to these two diseases, he does not believe that multiple sclerosis has its origin in syphilis, either hereditary or acquired. In syphilitic pseudosclerosis, the conclusions reached by spinal fluid examinations are absolutely different from those resulting from a study of the fluid in true multiple sclerosis. The Wassermann reaction on the spinal fluid is always negative in multiple sclerosis. Of course it must be admitted that among the hundreds of patients suffering from multiple sclerosis, there can easily exist a certain number who are syphilitic. In that case, however, we are dealing with two coexistent diseases without any necessary relationship. Moreover, there is no resemblance between the pathologic anatomic lesions of the two diseases. The only argument given by those authors who accept a syphilitic origin for multiple sclerosis is the presence in the histologic sections of perivascular plasmolymphocytic infiltrations. The writer insists, however, that these infiltrations are common and not sufficient to establish a syphilitic etiology. The syphilitic origin of multiple sclerosis has been rejected by Oppenheim, Marburg and the American Association of Research in Nervous and Mental Diseases. The author accepts this as an absolute conclusion.

Relationship of Multiple Sclerosis to Epidemic Encephalitis.—Proof exists in the literature that epidemic encephalitis finally leads to multiple sclerosis. The author insists, however, that among patients suffering from multiple sclerosis he has never seen the so-called Parkinsonian syndrome. Moreover,

in no case of epidemic encephalitis has he ever found a positive benzoin colloidal reaction. The lesions in epidemic encephalitis either early or late are different in their location and appearance from those of multiple sclerosis. He admits that he has had some cases of multiple sclerosis with somnolence, but somnolence is not necessarily pathognomonic of epidemic encephalitis.

Relation of Multiple Sclerosis to Acute Ataxia.—Acute ataxia is a rare condition, with pyramidal cerebellar symptoms which resemble those in multiple sclerosis, such as an ataxic spastic gait, dysmetria, intentional tremor, clonus, etc. Acute ataxia apparently follows various infections, known or unknown. Peck, Claud and even the author himself in his earlier work thought that acute ataxia might be the origin of a late multiple sclerosis, but he has had to give up the hypothesis. Acute ataxia in the course of a few weeks or months shows complete recovery without relapse.

The Spirochete Described in Multiple Sclerosis.—The author treats this study under three main heads: positive, clinical and experimental observations. Negative experimental or clinical observations and research carried out at the clinic of the Saltpêtrière: First, positive, clinical experimental observations. Most of these observations are citations from the works of others, including Bullock, 1913; Steiner, 1914; Kahn and Steiner, 1917; Simons, 1918; Marinesco, 1919; Kahn and Steiner, 1920; Kalberlah, 1921; Gye, 1921; Adams, 1921; Pettit, 1922; Stephanopoul, 1923; Sicard, Parif and Lermoyez, 1922; Schlosmann, 1923; Jensen, Schroeder, 1923; Jarlow Rud, 1923; Adams, Blacklock, Dunlop and Scott, 1924. These reports give the varying results obtained by intraspinal inoculation, inoculation of the brain or peripheral nerves and other methods. Some are positive in a large percentage of cases, and others are negative. The second division of the author's "observations," concerns negative reports from a clinical and experimental point of view. Almost as many writers are cited as in the positive group, beginning as early as 1914 with the work of Siemerling and Racke, and running down to Noguchi, 1923, and that of Barre and Reys, 1924.

The Association for Research in Nervous and Mental Diseases in 1921 concluded that further study was needed on the spirochetal origin of multiple sclerosis. Noguchi reached the same conclusions.

Studies Made at the Clinic of the Salpêtrière.—The work of LaRoche and LeChelle, as well as that of Ivan Bertrand, was negative. The author's intern, Marquézy, did experimental work on nine patients, who showed definite signs of multiple sclerosis in the developmental state. From them, he inoculated a monkey and twenty-one rabbits. He used every method of inoculation of any value. A monkey was inoculated from a patient suffering with multiple sclerosis of four months' duration, and died twenty days later, having developed a slight paresis of the lower extremities. Necropsy showed no apparent lesion. Examination of the spinal fluid with the ultramicroscope was negative. This one experiment of Marquézy is typical of all the cases. In none of his experiments was he able to demonstrate the spirochete either in his animals or in the spinal fluid of his patients. In the central nervous system of dead rabbits, Bertrand and Marquézy found no lesion which was similar to that of multiple sclerosis.

The author states that he has reviewed the literature of the past ten years on the spirochetal origin of multiple sclerosis, and regrets that he cannot present a precise conclusion. The negative experiments have not the value of the positive experiments, for the reason that positive results cannot be rejected.

He thinks that the discussion of the subject cannot be considered as closed, and that further biologic reasearch must be carried out. He believes that new experiments sooner or later will demonstrate the nature of the virus in multiple sclerosis. This virus exists. It is a spirochete. Is it a filtrable neurotropic virus? No positive response can be given. He looks for the best results, not from rabbits and smaller animals, but from the larger animals, which are more like man.

These experiments, if they can be carried out in our laboratories, might prove useful in the prophylaxis and treatment of diseases of the nervous system.

JONES, Detroit.

DIFFERENTIATION OF THE NEURONS IN THE CHICK EMBRYO DURING THE FIRST FOUR DAYS OF INCUBATION. J. F. TELLO, Libro en honor de S. Ramón y Cajal **1**:205, 1922.

Tello has studied the early differentiation of the diverse groups of neurons in serial sections of chick embryos. Cajal's silver nitrate method after preservation in 50 per cent. pyridin was used for impregnation of the neurofibrils. Good impregnations are obtained in embryos after the third day of incubation, but they are not constant in younger embryos. The findings in this investigation are summarized by the author as follows:

"1. The neurons in the chick embryo first differentiated are those elements whose axons form the posterior longitudinal bundle, namely, the neurons of the nucleus motorius tegmenti of Edinger, which extends from Cajal's interstitial nucleus — its most cephalic origin at the level of the diencephalon — to the anterolateral column of the spinal cord, crossing through the interstitial nuclei of the medulla oblongata. This extensive longitudinal pathway begins to appear simultaneously in the diencephalon, myelencephalon and most cephalic portion of the spinal cord during the second half of the second day of incubation.

"2. Our observations show, in agreement with Bok, that all the motor nuclei, whether somatic or visceral, recognize a common origin in the nuclear column which develops in contact with the posterior longitudinal bundle, from the mesencephalon to the spinal cord, during the last hours of the second day of incubation. Furthermore, in different points of the medulla there arise simultaneously neurons for a somatic and a visceral nerve, as, for instance, the facial and the abducens. A similar process is observed along the spinal cord. In such places of joint formation of somatic-motor and viscero-motor neurons, the latter are usually placed internal to the former. In the medulla oblongata, development of visceral neurons is more precocious, while in the spinal cord the somatic-motor neurons develop earlier.

"3. The first motor nuclei to appear are those of the oculo-motor, trigeminus and the anterior radicular or somatic nuclei of the spinal cord. The nuclei of the fourth, sixth and twelfth pairs of nerves arise several hours later. The visceral nuclei of the seventh, ninth, tenth and eleventh pairs appear in the same order as the arches they supply. The migration of visceral neurons toward their ultimate position in the adult does not begin until the fourth day of incubation.

"4. The ventral nucleus of the trigeminus seems to constitute an exception among the nuclei of the motor nerves since it is found lateral to the point of emergence of the nerve during the first hours of incubation.

"5. In a similar way, in the tegmental column and dorsal longitudinal pathway, where two centers of development exist in the motor column there are two centers — one anterior, mesencephalic, and one posterior, located in the uppermost portion of the medulla. The evolution of the neurons begins in these centers and descends along the neuraxis; in the upper traject, the descent is very rapid, taking place in less than twenty-four hours, while in the medullary portion it lasts more than two days, there being several hours of difference in the appearance of the diverse elements.

"6. Although it seems highly probable, as suggested by Bok and Kappers, that the development of the motor column is closely related to the evolution of the posterior longitudinal bundle, we believe that the path of the axon must be conditioned by the development of the organs to be innervated and the formation of the ganglia. The differentiation of neuroblasts under the influence of the posterior longitudinal bundle can be easily understood; in this way the motor column is produced. But, is this sufficient to explain the reason why some axons belonging to the same group, viz., facial and abducens, abducens and glossopharyngeus, accessory and hypoglossus, as well as all the axons in the cord, travel outwards (visceral) while others follow a ventral direction (somatic)? The somites and the ganglia seem to constitute powerful centers of attraction for the axons of the motor neurons, and the latter will follow one or the other direction according to the element which predominates at the moment in which the corresponding motor neuron is developing.

"7. The sensory ganglia of the cranial nerves develop successively in a descending direction beginning at the close of the second day; the cells in the neural crest are the most important element in the make-up of these ganglia. The epibranchial placode of the ganglion of the trigeminus must be of small importance and must develop very early, since we have not seen it clearly in good series. The placodes of the intermedius and glossopharyngeus are prominent, while the placode of the vagus is less important, although it is visible in the slides. Without attempting for the present to ascertain the influence of the epibranchial placodes on the formation of the ganglia in the chick, it seems to us that the authentic ganglionic elements arise in the neural crest, while the placodes must be concerned in the formation of other structures related to those of purely nervous nature.

"8. The development of the ganglia must coincide with the development of the alar portion of the base of the neural tube. Longitudinal growth seems to predominate in the first moments, producing the posterior longitudinal bundle, which serves as the axis around which develop all the other longitudinal pathways. The latter place themselves anterior and lateral to the bundle in the order of their appearance. After this initial stage there is transverse growth throughout the whole length of the central nervous system, the greater part of the commissural fibers and the motor visceral pathways appearing at the same time; the former arise from neuroblasts in the alar region, and after traveling in the base of the plate in a lateromedial direction, cross the midline and become longitudinal in the opposite side. The formation of commissural fibers takes place earlier in the bulb and spinal cord than in the other regions of the neuraxis. The notable development of the alar portion in the metencephalon and, especially in the isthmus, seems to influence the course of the axons of the trochlear nerve in a caudodorsal direction; decussation of these axons takes place on fusion of the lateral folds, and when this decussation takes place the axons continue their primitive direction, crossing the midline and emerging through the opposite side.

"9. The primitive diencephalic commissure (ventral supraoptical commissure or Gudden's commissure) is formed in front of the great longitudinal pathway, owing to the cephalic flexure of the neural tube in such a way that the striatothalamic tract appears in this moment as a bifurcation directed in front and upward. This commissure (Gudden's), crossing the midline in front of the inferior portion of the root of the optic peduncles, serves as a conductor of the optic fibers arriving from the retina, carrying them to the mesencephalon, after crossing that portion of the diencephalon which later forms the geniculate bodies. It is possible that, as in the case of the trochlear nerve, the direction of the fibers as they reach the decussation is the chief factor in their crossing over.

"10. After the formation of the interstitial segmental nuclei — especially those which are homolateral — sharing in the formation of the posterior longitudinal bundle, the alar or commissural nuclei appear. Then on the ventral surface of the myelencephalon homolateral neuroblasts undergo differentiation; their axons become longitudinal on the ventral surface, between the posterior longitudinal bundle and the groove for the mixed nerves. Behind this groove the neuroblasts are condensed in a well delimited nucleus constituting the sensory nucleus."

NONIDEZ, New York.

PATHOLOGY OF MYXEDEMA. M. G. MARINESCO, L'Encephale **19**:265 (May) 1924.

In this paper is given a detailed study of the nervous system and other organs in a case of myxedematous idiocy due to congenital absence of the thyroid gland. The patient was a girl, aged 15, at the time of her death. The family history was negative. The patient was the first child. Her general development was markedly retarded. She did not walk until the seventh year, and speech was only rudimentary.

The child first came under observation when 13 years old. Physically, she showed a relatively large head and small trunk. The anterior fontanelle had remained open, the milk teeth persisted, and all the teeth were poorly spaced. The neck was short, and its size seemingly increased by large pseudolipomas in the subclavicular spaces. The tonsils were large. The thyroid was not palpable. The lower half of the thorax was large, and the abdomen was of the "frog belly" type. The limbs were short, cold and cyanotic. The skin and subcutaneous tissues were thickened. There was no pubic hair. The roentgen-ray showed delayed ossification. The rectal and axillary temperatures were subnormal. There was slight anemia, and differential white cell count revealed 64 per cent. of polymorphonuclear cells, 24 per cent. large lymphocytes, 9.5 per cent. small lymphocytes, 2 per cent. eosinophils and 0.5 per cent. basophils.

Mentally, the child was an idiot. She had no spontaneous speech, did not know the names of her parents, and used the term "father" for all men. She could count only to 4. She was distractible and easily irritated or made to cry. Her gait was slow and hesitant.

A piece of thyroid gland obtained from a patient of the same age was grafted into the abdominal wall. A few days later, the child seemed brighter; she retained names better, and showed a larger vocabulary. Movements were more active, appetite was better, and temperature was nearly normal. The graft atrophied after about six weeks, and the temporary improvement disappeared. There were no changes in the bones visible to roentgen-ray examination as a consequence of the graft.

After various illnesses, the child died, two years later, with a generalized tuberculosis. Postmortem examination revealed a generalized miliary tuberculosis. The lungs showed the presence of bronchopneumonia, and the bronchial lymph nodes were enlarged. The subclavian artery was malformed. There was atrophy of the suprarenal cortex, and the ovaries and the uterus were infantile. There was delayed union of cartilages. The nervous system showed a tuberculous meningitis, and there were miliary nodules in the cortex and corpus striatum.

A microscopic study of the entire nervous system, using various stains, was made. Control sections of the normal brain of a child the same age were used. Allowance was made for the tuberculosis present in the case of myxedema, and sections were taken chiefly from areas not affected by tuberculosis. A comparative study of the various areas of the cortex and their cellular structure was emphasized.

In general, cellular development of all the cortical layers was retarded, yet the cells of the archipallium were not much different from the normal. The cells of all layers of the cortex were diminished in volume — the granular layer suffering the least. In the basal nuclei, there was a decreased volume of the cells but no evidence of changes of cell structure or of fibers. In the corpus striatum, there was an infiltration of vessels in the globus pallidus, with a characteristic iron stain in the muscular portion of the vessel walls. In some areas, the vessel walls showed granules stained by thionin and hematoxylin. The same stains showed such granules in small vessels and in capillaries which were at times obliterated by the deposits. These deposits or concretions were definitely not of calcium. In the substantia nigra, especially in the reticular substance, there were similar deposits.

Marked changes had occurred in the cerebellum. The Purkinje cells were small, elongated and not in their usual position with respect to the cell layers. Their dendrites were decreased in number. In general, the cerebellar cortex was reduced in richness of cells and fibers. In the white substance of the cerebellum, the capillary walls were infiltrated with granules staining with Prussian blue. They were particularly prominent in the dentate nucleus.

Cells of the hypoglossal nerve root and of the anterior horns of the spinal cord were decreased in size. Sections of the spinal ganglia showed the presence of glycogen granules both in the cell cytoplasm and in the axons. These granules occurred throughout the gray substance of the cord, and in the white substance they were deposited especially in the vessel walls. The dorsal root of the vagus and the olive contained no granulations. In the cortex, the superficial tangential fibers were arrested in development, and other association fibers were decreased in number.

Outside of the nervous system all the tissues showed a reduced volume of parenchyma, but some had large vesicular nuclei containing globules and were decreased in chromatin content.

Summarizing the pathology of the central nervous system, the author states that the cortex and basal ganglia were particularly involved. The persistence of Cajal cells in the hippocampus and other areas, and the reduction of volume of the subgranular layer of cells are evidence of arrested development.

The subnormal temperature has an effect in reducing all metabolic activities, and it is possible that the presence of glycogen granules in the various portions of the nervous system is due to an incomplete and sluggish oxygenation.

Hyslop, New York.

CONCERNING THE "SLEEP CENTRE." FRANZ LUCKSCH, Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:85 (Sept.) 1924.

A German, aged 27, entered the hospital with the history of having had a fever for two weeks. His illness set in with an articular rheumatism which was contracted as the result of a drenching. Physically, he showed a vegetative endocarditis, and complained of pain over the heart and in the left shoulder. About one month after the onset of his illness, the patient complained of severe headache and could find words only with difficulty. Two weeks later, he developed a profound lethargy, sleeping day and night. No paralyses were noted; the tendon reflexes were normal. After a time, he sat up in bed and took liquid nourishment, but immediately relapsed into his lethargic condition. Brudzinski, Kernig and Lasegue signs were negative. Several days later, a right-sided Babinski sign was noted, and a strongly positive bilateral Oppenheim sign. About two weeks after the onset of his lethargy, death followed. Bacteriologic examination of the blood in life showed numerous colonies of *Streptococcus viridans*. The clinical diagnosis was vegetative endocarditis; insufficiency of the aortic valves; pleural empyema; embolic focus in the wall of the third ventricle.

Necropsy showed a recurrent polypous endocarditis of the aortic valves with destruction of the left cusp; dilatation of the left ventricle and endocarditis of the mitral valves. The spleen showed many infarcts and an old gangrenous subphrenic abscess at the upper pole of the spleen. There were also several new and old infarcts in both kidneys and a fatty degeneration of the liver. The brain showed an embolic abscess of the gray matter of the third ventricle on the left side bordering on the hypothalamus and thalamus. There was also apparently fresh softening in the floor of the third ventricle and in the gray matter of this region on the right side and in the right hypothalamus. There was an irregular scar in the occipital lobe. Sections cut through the base of the brain at both extremes of the third ventricle demonstrated abscesses and coalescent areas of softening involving the gray matter in the posterior portion of the third ventricle and also the wall and surrounding territory of the beginning of the aqueduct. Smaller areas coming from the larger area of softening affected both mesial thalamic nuclei.

Pette describes a case of a man, aged 38, a heavy drinker, who became acutely ill with headache, vertigo and short periods of loss of consciousness. On entrance, he showed complete right oculomotor palsy, and an incomplete left and a slight right spastic hemiparesis. For three months, he was in a state of complete lethargy like that in epidemic encephalitis. Necropsy showed: an irregular, somewhat sunken but sharply defined grayish-yellow area between the substantia nigra and aqueduct on the right side, but not involving the red nucleus. On the left, this area involved the thalamus. Microscopically, the focus was made up of several small foci and consisted of glia tissue, cells and vessels. Pette stated: "The following is proved by this case. There is a locus in the gray matter of the floor of the third ventricle which has very significant relations to the function of sleep; apparently it is the sleep centre itself." The author finds both cases, that of Pette and his own, very similar clinically, in that both showed marked lethargy and both ended in death. In both cases, the lesion was in practically the same location — in the region of the oculomotor nerve, the aqueduct of Sylvius and the adjacent part of the thalamus (pulvinar).

In epidemic encephalitis, the gray matter of the third ventricle, the aqueduct and that in the floor of the fourth ventricle are especially affected, "and we

will from now on have to ascribe the lethargic states in the above-named illness to changes in the gray matter in the posterior portion of the third ventricle and about the aqueduct." Manthner, in 1890, called attention to a disease called nona, and stated that besides inflammatory changes in the walls of the third ventricle and of the aqueduct, nothing was found pathologically. He looked on normal sleep as a symptom of fatigue of the gray matter of the ventricles. Luksch says that sleep is produced by the fatigue of cortical cells either through products of intoxication or through use. By these processes the cells are thrown into inactivity. His conclusions are in agreement with those of Pawlow through the use of conditioned reflexes. In conclusion, he states that the lesions in the aqueduct and its vicinity are of great significance in explaining the pathogenesis of epidemic encephalitis.

ALPERS, Philadelphia.

THE RÔLE OF OXYDIZING FERMENTS IN THE VITAL PHENOMENA OF THE NEURON. G. MARINESCO, Schweiz. Arch. f. Neurol. u. Psychiat. **15**:3, 1924.

In carrying out this work, the newer methods of ultramicroscopy, vital staining and histochemistry have been used. In all nervous centers, oxydizing ferments exist only in the cytoplasm, in the dendrites and in the cone of origin of the axon. The granules may be found in the fine nerve terminals of the sensory endings and in the corpuscles of Meissner and Krause, of Pacini, Golgi, etc. They are also noted in the sympathetic ganglia which are devoid of a myelin sheath. Immediately on the appearance of the myelin sheath, the oxydizing ferments disappear. This general rule, however, has some exceptions.

The cerebral cortex offers a rather interesting topography with regard to these ferments. The neuroglia cells of the first layer do not contain them, but they are found in the nerve cells of the other layers of the cortex. In some of the larger cells, it is found that when pigment appears, the oxydases disappear. The older the animal, the greater the amount of pigment; it is therefore advantageous to study the ganglion cells of younger animals. It is found that in the lumbar ganglia of a young dog or rabbit, the entire cells are filled with oxydasis. It is further seen that there are clear cells and cells which are obscure; in the first, the dispersion of the oxydizing ferments is greater, and in the second, the granules approach each other so closely that it is difficult to distinguish them separately. Near the nodes of Ranvier, a characteristic border is noted, owing to the granular appearance of very fine oxydizing ferments. In the gray matter of the cord, the nerve cells are buried in the background of oxydizing ferments. No doubt these are located in the pericellular plexuses and take part in the formation of the synapses.

In nerve cells in which black pigment occurs, such as those of the locus niger and of the locus coeruleus, it is seen that oxydizing ferments occur in inverse proportion to the pigment. In infants, melanin is not found; however, this increases with age until in the adult the melanin granules almost fill the entire cell. This is also noted in pigmented areas of the skin, for example, in the areola of the breast, where one finds no trace of oxydizing ferments. These greatly pigmented cells seem to be relatively inactive physiologically.

There is a certain relationship between the development of the fuchsinophilic granules and that of the oxydases. In a 7 months fetus one finds an abundance of fuchsinophilic granules in the nerve cells; fuchsinophilic granules seem to be a measure of actively developing cytoplasm.

In the regeneration of nerves, oxydizing ferments appear. The activity seems to be governed by the temperature factor, and a great difference is noted in

the regeneration of nerves of poikilothermal and homothermal animals. In the frog, for example, the phenomena of regeneration are functions of the temperature.

The phenomena of neurotropism are probably dependent, at least in part, on the activity of oxydizing ferments.

In pathologic states such as amyotrophic lateral sclerosis, progressive muscular atrophy, the myopathies, etc., the process of degeneration goes hand in hand with a diminution of oxydases.

WOLTMAN, Rochester, Minn.

MALARIA AND DISEASES OF THE NERVOUS SYSTEM. G. W. PERWUSCHIN, Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:446 (Nov.) 1924.

An epidemic of malaria in Russia during the past two years gave the author an opportunity of observing the effect of this disease on the nervous system. During the acute stages, there is evidence of an effect on the nervous system, partly irritative and partly depressant. Headache, vomiting, pains in the back and muscles occur during the acute paroxysm. Epileptiform convulsions occur in some cases of malaria, and are characterized by unconsciousness and convulsions from the onset of the disease. With the increase in temperature, there occur convulsions, local twitchings, delirium or coma. At the end of the attack, one finds great weakness, twitching of the extremities and apathy.

In cases of chronic malaria, evidences of involvement of the nervous system are found in headaches, general weakness, vertigo and hyperkinesis of the upper extremities in the form of tremor of the hands or head. Neuralgia is a common sequence of malaria, and often the trigeminal nerve is involved. In seventeen cases of neuralgia after malaria, nine involved the trigeminal nerve, five the ischiadic nerve, two the brachial plexus and one the occipital nerve.

Peripheral neuritis after malaria has long been recognized. Of 252 cases of optic neuritis following infectious diseases, Uthoft found that seventeen cases followed malaria. The common finding is an amblyopia and more rarely an amaurosis which is not constant. In such cases, there is often a central scotoma or a narrowing of the visual field. Ophthalmoscopic examination reveals papilledema, retinal hemorrhages, chorioretinitis, inflammation and atrophy of the optic nerve and papilloretinitis. It is fairly common to find also a neuritis of the eye muscles or a complete paralysis of all the eye muscles of one side, or oculomotor paralysis. Neuritis of the facial nerve is not common. Neuritis of the ulnar, axillary, suprascapular, radial, musculocutaneous, peroneal and ischiadic nerves following malaria has been described. The author reports briefly a case of neuritis of the trigeminal and facial nerves and another of a polyneuritis with involvement of the facial nerve. Both cases followed malarial infection. According to the author, there are reported in the literature thirty cases of polyneuritis following malaria.

Italian investigators have described acute cerebellar disease following malaria, and the author reports three cases of this type. Diseases of the cerebrum are not common after malaria. Hemorrhagic encephalitis, epileptiform convulsions, facial palsies, palsy of the glossopharyngeal nerves and of the upper extremities have been recorded. Hemiplegia with motor aphasia and dysarthria has been reported following malaria. Acute psychoses have also been described. There is an extensive bibliography.

ALPERS, Philadelphia.

THE RESULTS OF SUBSTITUTING AN EXTRANEOUS MEDULLA FOR THE CEPHALIC END OF THE EMBRYONIC SPINAL CORD IN AMBLYSTOMA. S. R. DETWILER, J. Exper. Zool. **41**:293, (Feb. 5) 1925.

Replacing the first five segments of the embryonic spinal cord by a unit of neural tube, involving an extraneous medulla and the first two spinal segments in Amblystoma, brings about an increase in the size, volume and number of cells in the spinal segments caudal to the transplanted medulla. The cellular increase is most marked in the transplanted first and second segments which occupy the positions of the normal fourth and fifth, respectively, and becomes less marked in successive segments. The increased neuroblastic proliferation in the spinal segments caudal to the extraneous medulla appears to have been brought about under the influence of the additional caudally growing projection fibers arising in the extraneous medulla. The greatly increased number of cells in the transplanted first and second segments cannot be associated with functional needs at the periphery. It appears rather to be associated with the amplitude of stimulation coming from the projection fibers which terminate at these levels. The same applies to the intact sixth and seventh segments. The curtailed cellular development as found in the transplanted medulla as compared with that in the normal cephalic spinal segments which it replaces is attributed to the greatly lessened axonal ingrowth from the fragmentary cranial ganglia associated with the transplanted medulla. Ear vesicles which are transplanted with the medulla undergo various degrees of differentiation in the abnormal position. In several cases, localized groups of sensory hair cells were developed and were innervated by branches from the transplanted acoustic ganglia. In all cases, the cartilaginous otic capsule was fragmentary.

The early reactions of larvae with an extraneous medulla are in all essentials normal. Swimming reflexes are also of normal character. Defective function of the anterior limbs as found in these experimental animals is correlated with a general deficiency of nerve supply and with specific lack of innervation in certain shoulder muscles. In normal larvae, the brachial plexus is derived from the ventral rami of the third, fourth and fifth spinal nerves. In the experimental cases, it is derived mostly from the transplanted second nerve (which replaces the normal fifth) and the normal sixth. The latter contributes most of the nerve supply. In one case, the transplanted first nerve supplies the limb. The hypobranchial musculature may be entirely lacking in nerve supply or may be supplied from the transplanted first spinal nerve, or from both the transplanted first and second, in which case a typical hypoglossal nerve is formed. The extraneous medulla preserves its typical medullary configuration with remarkable completeness, suggesting that internal factors are mostly responsible for the ensemble.

WYMAN, Boston.

VARIATIONS IN VAGO-SYMPATHETIC TONUS IN CONFUSIONAL CRISES. TINEL and SANTENOISE, L'Encephale **19**:426 (May) 1924.

The authors present three cases demonstrating variations in the balance of the vegetative nervous system correlated with mood deviations. Each of three patients presented a state of confusional stupor with abolition or reduction of both the oculocardiac and solar reflexes. With clinical improvement, these reflexes returned. When agitation was present during the confusional state, the solar reflex was less apt to be retained. Each of the three

patients, on recovery, showed a preponderance of the autonomic as judged by various tests.

Clinically, the mental states were comparable to the psychoses due to infections and intoxications. However, it seems that in the confusional crises there is a decidedly strong effect on the function of the autonomic or parasympathetic portion of the vegetative nervous system. The authors affirm that the state of vagotonia is especially susceptible to intoxications and particularly to fixation of toxins in nerve centers.

One cannot help but wonder whether emotional instability may not in a way be parallel with vagotonia and that emotional stresses, in their effect on the vegetative nervous system, likewise predispose to intoxication.

HYSLOP, New York.

MUSCLE TEARS. A. GOTTLIEB, Arch. Surg. **9**:611 (Nov.) 1924.

In comparison with the detailed study given to rupture of muscles and avulsion of their attachments, little attention has been paid to muscle tears, i. e., injuries of the muscle substance with little disturbance of the continuity of the muscle. The latter have either remained unrecognized or have been taken lightly and disregarded.

Muscle tears occur more frequently in men than in women. They are more common in persons above the age of 40, when body elasticity and resiliency have lessened. Certain muscles may tear in the course of definite occupations. The mechanism responsible for the tear cannot always be established. A tear occurs in a contracted muscle when a sudden, poorly coordinated movement is executed in a moment of unawareness or surprise; it results from an unconscious act of protection against a threatening danger.

Since muscles will tear more readily if tired from overuse, the state of fatigue of the muscle at the time of the accident, as well as the general health of the person, must be considered. Sufferers from syphilis, arteriosclerosis, arthritis deformans, acute infectious diseases, alcoholism and other constitutional defects are more likely to sustain this as well as any other injury.

The onset is sudden, accompanied by a severe sharp pain, as if a knife had pierced the region. As a rule, the person instantly stops all activity in the injured part. An audible and perceptible crack may accompany the tear. The objective signs vary with the location and the degree of the tear: there will always be tenderness on pressure over the site of the tear and increase of pain if the motions executed separate the torn fibers. A groove or a depression in the muscle substance may not always be palpable, and ecchymosis from capillary hemorrhage may be present if the tear is superficial.

The treatment aims not only to restore function but also to guard against muscle atrophy. This being essential in all muscle injuries, it is particularly essential in affections of the quadriceps which, of all muscles in the body, is the quickest to waste. Physiotherapy should therefore be administered at the earliest date. Walking with a limited range of flexion should be encouraged; violent exercises, interdicted. Strapping with adhesive to hold the torn fibers in approximation and to limit the amount of flexion should be practiced. Failure after four weeks of conservative treatment may serve as an indication for the suturing of the torn muscle, which is to be followed immediately by physiotherapy.

Three case reports are included. GRANT, Philadelphia.

A Quantitative Study of Reactions to Light in Ameba. H. T. Folger, J. Exper. Zool. **41**:261 (Feb.) 1925.

Ameba responds to a sudden increase in illumination by complete cessation of movement an appreciable time after the light is increased. There are marked individual variations in this reaction time, but the variations are not so great in ameba of the same culture as in those of diverse cultures. The latent period between stimulation and response may be spent either in darkness or in light. At any given intensity, the reaction time, the latent period and the stimulation period usually remain practically constant, although changes may occur. The reaction time varies inversely with the luminous intensity. The latent period is comparatively short in a very strong light, but increases in length as the intensity decreases until a maximum is reached, beyond which it decreases. The amount of light-energy received during the stimulation period decreases as the illumination decreases until a minimum is reached, beyond which it increases. The minimum is found in the same intensity as the maximum latent period. The latent period and the stimulation period may be calculated from reaction times. In order to obtain a response after an ameba has once responded to a sudden increase in illumination, a certain length of time, usually from one to two minutes, must elapse. The first part of this period may be spent either in darkness or in light. The latter part, usually from ten to twenty seconds, must be spent in darkness or in a lower intensity. The processes acting during this time are known as dark adaptation. Incomplete dark adaptation is manifested by an increase in the reaction time or by failure to respond. A slight mechanical shock causes the reaction time of the response to an increase in illumination immediately following it to be longer than usual. If the shock is so heavy as to cause a retraction in the pseudopods, an increase in illumination just as the animal is recovering results in an exceptionally short reaction time. This indicates that increase in illumination and mechanical shock produce the same changes in ameba, and that mechanical stimulation and photic stimulation are fundamentally the same. If this is true, it is evident, since mechanical stimulation is not photochemical, that photic stimulation cannot be photochemical. An ameba which is forming a food cup invariably fails to respond to a sudden increase in illumination. After the food cup is formed, however, the stimulation period and the reaction time are often shorter than usual. Temperature apparently exerts little if any effect on the reaction time.

Wyman, Boston.

Structure of the Nucleus Dentatus. A. Gans, Ztschr. f. d. ges. Neurol. u. Psychiat. **93**:750 (Nov.) 1924.

Contributions on the structure of the dentate nucleus have been relatively few. Weidenreich found only a round, poorly developed clump of cells in a five months old human fetus in the region of the dentate nucleus. In a fetus of 6 months, he found the dorsal portion of the nucleus differentiated better than the ventral part, and characterized by two folds. Astwatzaturow and Vogt found that the dentate nucleus was fully developed in a 7 months fetus. Van Valkenburg found only the dorsal portion of the dentate nucleus myelinated in a 42 cm. fetus. Horsley and Clark found that the frontal portion of the dentate nucleus influences movements of the eyes and head, while the other portions influence movements of the limbs. Brouwer found that the postero-inferior portion of the dentate nucleus contained no fibers, whereas the dorsal portion did. Gans was able to confirm this by means of the iron

reaction, demonstrating that the postero-inferior portion of the dentate nucleus stains with this reaction, whereas the medulla of the cerebellum and the other portions of the dentate nucleus are not stained or react weakly. Guizetti, who studied the dentate nucleus by means of the iron reaction, reports also that the lateroventral portion of the nucleus stains more deeply than the other portions. A more exact interpretation of these findings would be that the cells of the nucleus dentatus react more strongly in its ventral portion than in its dorsal portion. The medulla is stained, but less clearly and only in the ventral portion of the nucleus.

The author made comparative studies of the nucleus dentatus in the chimpanzee and in man. There is very little difference in the structures of the nucleus in these classes. In *Cebus capucinus*, the dorsal portion is smaller than the ventral portion. The dorsal portion of the nucleus has larger cells, which are widely separated from one another by fibers. In *Cebus fatuellus* the dorsal portion is relatively smaller than in *Cebus capucinus*. The cells of the dorsal portion are larger and more widely separated than those of the lower portion. In *Lemur catta* there is little difference between the dorsal and ventral portions. In man, the ventral portion of the nucleus, as stated above, stains with the iron reaction, while the dorsal portion remains unstained or stains weakly.

ALPERS, Philadelphia.

THE DYNAMIC COMPONENTS OF THE CEREBRAL HEMIPLEGIAS. OTTO MARBURG, Folia neuropath. Esthoniana, Festschrift Prof. L. Puusepp **3**:11, 1924.

Three components in hemiplegia must be differentiated: the kinetic disorder, or limitation of voluntary movement, the tonostatic disturbance, leading to hypertonia, which is lacking in some cases of extensive lesion of the frontal lobe, and the dynamic. The dynamic component has received little emphasis, but it is found that even in severe paralysis actual muscular power is relatively little diminished. The force with which the paralyzed hand is clenched into a fist in old severe cases of hemiplegia differs markedly from case to case. In the usual case, there is kinetic-hypertonic-dynamic paralysis, but there may be only a kinetic and hypertonic loss, the dynamic power being retained. In the atonic hemiplegias, the dynamic power is also lost. Power and tonicity are not always coincident, as is observed in the striate syndromes. Cerebellar paresis with its hypotonia "is nothing but hypodynamia, a disturbance of basic force." Pontile lesions are accompanied by great spasticity and hyperdynamia, and cerebellar lesions with hypodynamia. Thus we see that in the pontocerebellar system there is a projection tract concerned with dynamic factors.

Hemiplegia is severe in pontile lesions, because the pyramidal tract is collected into a small bundle and is involved in toto. It is also severe because obviously here the dynamic tract is affected in its two parts, the tegmental and the cerebellar.

For this dynamic system we can postulate a tract arising in the frontal and temporal lobes traversing the internal capsule and the basis pedunculi where it divides into a pontile portion and a cerebellar portion, the former reaching the cord directly and the latter indirectly. The author believes that the dynamic tracts in the cerebellum are to be considered as controlling the amount of force carried to the muscles.

Cerebral hemiplegia can take on at least three forms: first, a complete form in which all three components are present (kinetic, tonic, dynamic); second, the kinetic-hypertonic form in which the dynamic aspect is well preserved;

and third, a kinetic-hypotonic-adynamic form, in which, together with the disturbance of tonus, there is a similar one of the dynamic component.

FREEMAN, Washington, D. C.

CELL AND ALBUMIN CONTENT OF NORMAL SPINAL FLUID. AXEL V. NEEL, Schweiz. Arch. f. Neurol. u. Psychiat. **15**:70-96, 1924.

A survey of the literature shows at once that the results of the study of normal spinal fluid varies considerably according to the country, the type of material available and the methods used. Neel wished to avoid all factors which might result in error. In order to do this, the laboratory worker was kept in ignorance of the case from which the spinal fluid was obtained; punctures were made with patients in different positions; the fluid was divided for different tests, now this way and now that; as a rule, from 4 to 6 cm. were withdrawn; the Fuch's Rosenthal counting chamber was used. His earlier conclusions led him to the belief that 6-3 represented the maximum count obtained under normal conditions.

The albumin test was made with ammonium sulphate and potassium sulphate, according to Ross-Jones-Brandberg-Bisgaard, and the globulin estimation according to Buillain-Nonne-Apelt-Schumm. The Pandy method was used by the author, who endorses it heartily and thinks that when it is negative, a pathologic increase of albumin does not exist.

The analytic study of entirely negative cases showed a cell count of 0 to 1-3, globulin 0, albumin under 10. When the patient gave a history of syphilis, these findings were often increased. The author believes that there is always some reason when the cell count or albumin content exceeds the foregoing figures. In about 7 per cent. of cases, there was an increase in cells above 1-3; Neel believes this can be explained by our inability to demonstrate clinically that these cases are absolutely normal. He believes that fully 82 per cent. of syphilitic patients have involvement of the nervous system.

WOLTMAN, Rochester, Minn.

THE CORRELATION OF RECENT ADVANCES IN CEREBRAL STRUCTURE AND FUNCTION WITH FEEBLEMINDEDNESS AND ITS DIAGNOSTIC APPLICABILITY. R. J. A. BERRY, M. J. Australia **1**:393 (June 7, Suppl.) 1924.

Berry traces the development of the central nervous system from the primitive mammals upward and calls attention to the fact that the final step in the centralization of the nervous mechanism is reached with the addition of the psycho-associational neuron and attains its highest development in man in the supragranular cortex of the association areas. It is well known that both the supragranular and infragranular cortices differ in thickness in man, either from errors of development or from disease. It is not so well known that the differences in the relative development of these two cortices give different reactions to social environment. Since the supragranular layer is the last to develop, it is the first to undergo retrogression. Its width varies in normal brains and is measurably thinner in patients suffering from dementia. In a group of 355 criminals, Berry found the cubic capacity of the skull small. He argues that this is due to the lack of development in the supragranular cortex and results in a corresponding deficiency in the ability of these persons to control their lower instincts (infragranular cortex). The author notes that there were 176 unskilled crimes and only nineteen that might be classified as

skilled crimes in this group. He concludes that no one except a well trained neuropsychiatrist, after the consideration of a carefully taken history, a complete physical, neurologic and psychiatric examination, including the various so-called psychologic tests, has any right to diagnose or prognosticate the future in any case, especially that of a child. Cases are quoted to illustrate this point.

POTTER, Akron, Ohio.

OPERATIONS ON NERVES. A. A. JARIZYN, Folia Neuropath. Esthoniana **3**:199, 1924.

In the Neurosurgical Institute of Petrograd, during and after the war, 275 operations were performed on the peripheral nerves. From a study of these, the author draws the following conclusions:

1. A damaged or scarred nerve trunk cannot regenerate and must be operated on if paralysis, contracture or pain is present.

2. A complete anatomic or physiologic break demands suture in every case.

3. The neurosurgeon must decide on the type of operation.

4. Tubulization, neuroplasty, anastomosis and transplantation must be discarded as operations that cannot facilitate the regeneration of nerves.

5. Endoneurolysis, since it cannot accomplish the full regeneration of a nerve, is to be condemned. Resection of the altered portions and subsequent suture is the best operation in trophic disturbances.

6. Embedding the suture in a location rich in connective tissue is needless. The nerve may be left in its normal place.

7. In suturing, the nerve must be freshened until the normal nerve bundles appear.

8. The end point of the possibility of regeneration has not yet been established; therefore it is never too late to perform the operation.

FREEMAN, Washington, D. C.

TREATMENT OF GENERAL PARALYSIS OF THE INSANE BY MALARIA. H. J. MACBRIDE and W. L. TEMPLETON, J. Neurol. & Psychopath. **5**:13 (May) 1924.

The following method of treatment was used: Subcutaneous or intravenous injections of 2 to 4 c.c. of venous blood from a patient suffering with benign tertian malaria were given (the strain should be renewed as frequently as possible, since the virulence tends to increase with each successive human transmission). The patients were permitted to suffer an average of twelve pyrexial attacks, after which the fever was terminated with quinin. In addition, six weekly doses of one of the arsenic preparations were given. The results in eighteen cases follow: Two persons with juvenile general paralysis showed no improvement; of five with chronic cases, one died during the fever, and four showed some degree of mental and physical improvement; of eleven with early cases, two died during the fever, three showed marked mental and physical improvement, three showed considerable improvement, more physical than mental, one became worse and had to be certified, and one showed slight mental but no physical improvement. These authors are not enthusiastic over the results they were able to obtain in this short series, but believe the treatment should be tried especially in early cases.

POTTER, Akron.

STUDIES ON THE RETINA. OBSERVATIONS ON THE RODS OF NOCTURNAL MAMMALS. S. R. DETWILER, J. Comp. Neurol. **37**:481 (Oct.) 1924.

There are no observations to show whether light effects any structural changes in the mammalian rods. Though the cones of the verebrate retina generally shorten in the light, the rod does not behave so uniformly. If active at all, its most typical response is a lengthening of the myoid in the light. The retinas of the field mouse and bat, which are noctural animals, possess very slender cylindrical rods and no cones. These rods do not show any positional changes in response to stimulation by light. The epithelial pigment is scanty, and it also shows no migration under the influence of light. These and previous experiments prove that the mammalian retina shows very slight mechanical changes in response to light, or none at all. These phenomena which take place so extensively in the lower vertebrates apparently cannot be included as essential factors in any theory of vision or as participating in the retinal adaptation in mammals.

C. J. HERRICK, Chicago.

DEMENTIA PRAECOX (CHRONIC HYPOTHYMIA). R. BENON, Schweiz. Arch. f. Neurol. u. Psychiat. **15**:140, 1924.

Esquirol, in 1814, was the first to refer to this condition as a "dementia." Morel, in 1852, used the expression "juvenile dementia," and in some of his articles called it "dementia praecox." Kalbaum, in 1863, created the expression "hebephrenia." Kraepelin, in 1893, referred to it as "dementia praecox." Régis, in 1906, referred to this condition as "chronic mental confusion." Bleuler, in 1911, called it "schizophrenia." Benon, in 1916, referred to it as "chronic hypothymia," believing that the malady does not concern intelligence, but that it is a disease of the emotions.

It does not appear to be an established fact that intellectual enfeeblement is fundamental to the conception of dementia praecox. On the contrary, emotional indifference is extremely marked. There are sometimes violent, impulsive reactions, but only at intervals. Dementia praecox may appear in the form of stupidity, with catatonia, mania and as delirium. The author does not believe that this disease can be considered a dementia, but should be regarded as a dysthymia.

WOLTMAN, Rochester, Minn.

BASAL PULSE RATE AND PULSE PRESSURE CHANGES ACCOMPANYING VARIATIONS IN THE BASAL METABOLIC RATE. J. MARION READ, Arch. Int. Med. **34**:553 (Oct.) 1924.

The author studied the relationship of pulse rate and pulse pressure to the basal metabolic rate, and found that the pulse rate varied directly with the basal metabolic rate, and that the pulse pressure also varied directly with the basal metabolic rate. In this way, he was able to derive a formula by which the basal metabolic rate could be determined simply from the pulse rate and the pulse pressure. The formula is as follows: $B.M.R. = 0.75 (P.R. + 0.74\ P.P.) - 72$. B.M.R. is the basal metabolic rate, P.R. is the pulse rate and P.P. the pulse pressure. This method, the author finds, will give the basal metabolic rating within 10 per cent. of its correct value in slightly over half the cases, and is therefore sufficiently reliable when frequent determinations with the respiration calorimeter are not practicable.

VONDERAHE, Cincinnati.

SOME EXPERIMENTS ON THE TRANSPLANTATION OF THE OLFACTORY PLACODE IN AMBLYSTOMA. H. SAXTOM BURR, J. Comp. Neurol. **37**:455 (Oct.) 1924.

In very early embryonic stages an extranasal placode was grafted in beside the normal placode. The transplant may or may not fuse with the placode of the host, and from the neuro-epithelium of the transplanted placode nerve fibers arise which may follow any one of four courses. They may join the normal olfactory nerve; they may reach the cerebral hemisphere in more or less aberrant ways; they may pass back to the region of the thalamus, here pierce the cranium and penetrate the dorsal part of the thalamus through a slight ganglionic enlargement; they may join the ophthalmic division of the fifth nerve. The third of these cases takes a course which has no precedent in normal animals. It seems to be a new nerve terminating in a part of the brain with little or no olfactory connections. The author suggests that these fibers may represent an aberrant nervus terminalis, but this seems out of harmony with the known course of the latter nerve.

C. J. HERRICK, Chicago.

THE DEVELOPMENT OF SENILE PLAQUES. L. BOUMAN, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:267, 1924.

Most brains that show senile plaques show them in the terminal stage, but Bouman's case showed them in the process of formation. They begin as minute areas of softening near small vessels. The earlier plaques are homogeneous, bean-shaped, hyalinized areas, apposed to the vessel by the concave side. Sometimes they encircle the vessel, but remain larger on one side resembling a seal ring. Along vessels cut longitudinally they appear as interrupted bands without actual fusion. In development, the masses take on a brushlike form, the streamers springing from the outer aspect. The fully developed plaques show this radial arrangement, the vessel being located somewhat eccentrically. The author believes that most of the plaques develop at a definite time in the life history of the individual, and that this explains the usual finding in the fully developed forms.

FREEMAN, Washington.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 23, 1925

CHARLES W. BURR, M.D., *President, in the Chair*

PSYCHOSIS ASSOCIATED WITH TRAUMA OF THE HEAD SUSTAINED IN INFANCY AND DETERMINING A LATER DEVELOPING DURAL TUMOR. DRS. A. E. TAFT and E. A. STRECKER.

This paper will be published in full in a later edition of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY.

A CASE OF ASTEREOGNOSIS PROBABLY OF PERIPHERAL ORIGIN. DR. ALFRED GORDON.

A woman, one and one-half years ago began to have pain in the left arm. This was soon followed by an awkwardness in the fingers. The condition gradually increased, and she was soon unable to perform the finer movements with the hand.

Examination revealed that the entire left arm was somewhat smaller than the right, but especially the forearm, wrist and hand, although the power of the forearm and arm was good. The grip of the left hand was only fair. The interossei muscles were much involved, as adduction of the fingers could not be carried out easily unless the entire hand was bent downward. The biceps and triceps reflexes were increased in the affected extremity.

Superficial sensibility was greatly involved, particularly on the hand, and less pronouncedly on the forearm where the patient made errors in spot localization. There were times when she did not recognize pin-prick and touch on the posterior aspect of the hand and forearm. The patient made gross errors by taking cold for heat and vice versa, more on the hand than on the forearm. The position of the fingers when manipulated by the examiner was not recognized by the patient, and the recognition of the two points of the compass was at times possible and only when they were widely separated. The stereognostic sense was strikingly affected — the patient was unable to recognize the material and the consistency of objects, nor could she name them when they were placed in her left hand. The movements of the fingers of the latter were awkward; she could not hold an object for any length of time, and she did not know when it left her hand.

Pressure over the inner aspect of the arm near the axilla provoked exquisite pain, and the patient complained of pain in that area when the arm was in motion. The affected hand was always in motion; the fingers were constantly in action. In every other respect, the patient's health was normal, except that she was very emotional. The eyes, sphincters and tendon reflexes were all normal. Biologic tests of bodily fluids were negative.

To sum up: We are dealing here with a case of astereognosis of one hand associated with an involvement of the superficial and deep sensibilities. As to the origin of this phenomenon, it cannot be central, as there has never been a symptom or a disturbance of any kind that could be referred to the cortex, subcortical tissue, thalamus, pons or peduncle. There is no evidence

of a Brown-Séquard syndrome, of tabes or of syringomyelia. Radiculitis could also be eliminated, as in such cases the astereognosis would have been of the radicular type, i. e., it would have been confined to one or two fingers. The tenderness of the brachial plexus and the subjective pain experienced by the patient in the same area point to a peripheral lesion, i. e., neuritis. The involvement of the interossei lead to the possibility of an ulnar neuritis being the cause of the sensory disorders and of the astereognosis.

A Case of Incipient von Recklinghausen's Disease. Drs. S. S. Greenbaum and C. A. Patten.

The case presented was interesting from the standpoint of excessive pigmentation without the neurofibromatosis usually encountered in this disease. The family history was negative. The patient was a full term, breast-fed baby, growing very slowly until the age of 15. She was backward at school, reaching the eleventh grade in ten years. The mother stated definitely that the patient had had six or seven sets of teeth. Her periods began at 15, and had been regular. She had been employed successfully during the last year or two, at a low wage. The mother said that the patient had a very poor memory, particularly for recent events. She had never been enthusiastic regarding boys, and apparently had very little sex feeling. At the age of 6, she had had measles, followed by jaundice; the mother marked this as the beginning of the pigmentary disturbance, and since that time, the areas of pigmentation had been gradually extending, until they are now very large.

Examination revealed a short girl, very well developed, with a great deal of doughy fat, very dry hair, carious teeth and dry, harsh skin. Beginning around the lower part of the face, behind the ears and on the neck, there were areas of brownish pigmentation varying in size from that of a pinhead to 4 inches (10 cm.) in diameter. There was more pigment on the exposed surfaces than elsewhere, but there was a great deal also on the covered parts of the body, more marked, however, on the chest and back than on the lower extremities. The patient's blood test, on one examination, was positive for syphilis, but the tests made on her mother and the rest of the family were negative. The patient denied exposure.

From a dermatologic standpoint, four cardinal signs or symptoms in von Recklinghausen's disease were recognized. They were in the order of their importance: pigmentation, cutaneous fibromas, neurofibromas and mental disturbances. This patient showed lenticular and hepatic areas of pigmentation, with a rather dull mentality, which put her in the group of incipient or abortive cases. There were several points of interest from an endocrine standpoint, which have been rather well summed up by Tucker (Von Recklinghausen's Disease, with Especial Consideration of Endocrine Connection, Arch. Neurol. & Psychiat. **2**:308 [March] 1924) and Levin (Recklinghausen's Disease: Its Relation to the Endocrine System. Report of an Illustrative Case, *Arch. Dermat. & Syph.* **4**:303 [Sept.] 1921). Tucker states that no evidence was found of involvement of the thyroid, parathyroid or pancreas in his cases, but that most frequently the pituitary gland was involved. In nine of the cases, three were acromegalic and one hypopituitary. The suprarenals were nearly always involved, and all except one showed pigmentation. Necropsy in one case revealed a definite degeneration of the suprarenals.

Levin's patient showed involvement of the suprarenals, pituitary, thyroid and gonads.

TWO CASES OF GENERALIZED ALOPECIA; ONE WITH NECROPSY FINDINGS. DRS. GEORGE WILSON and N. W. WINKLEMAN.

This paper will be published in full elsewhere.

NEW YORK NEUROLOGICAL SOCIETY

The Four Hundred and Eighteenth Regular Meeting, Feb. 3, 1925

E. G. ZABRISKIE, M.D., *Presiding*

A CASE OF INDUCED EPILEPSY. DR. B. ROSENBLUTH.

This case was presented in order to bring out an interesting point in the study of epilepsy. The illness of a man, aged 54, had begun fourteen years before presentation. At that time, he had been in Beth Israel Hospital with a disease diagnosed as cerebral thrombosis. The case was characterized by a slowly developed left hemiparesis with slight deficiency in speech and writing. Besides, there was a diminution of pain, touch and temperature sense over the major portion of the same half of the body. There was no rise in temperature. The blood counts were normal. The urine was normal. The Wassermann tests of the blood and cerebrospinal fluid were negative. The duration of his illness at that time was more than ten weeks.

Dr. Rosenbluth saw him eight years after his first attack, when he had a recurrence of his weakness on the same side. Besides weakness, the man had a positive Romberg sign, being thrown backward or sidewise. There were no sensory disturbances and no aphasic phenomena. The most interesting feature was the result of attempts at volitional acts with the arm or leg or eyelids. After the first effort, the arm or leg would be thrown into a convulsive attack of a chronic nature limited to the limbs that were in action. The same thing occurred when a periosteal or tendon reflex was tested on the left side. At this time, the face became slightly flushed, and the man's manner became confused.

In January, 1925, he had headaches and dizziness, with psychic insomnia. He had not been able to work for two years on account of a minor accident to his affected shoulder. He had always been left-handed. Mentally, the man was alert and spoke well; his station and gait were normal with the eyes open. There was a positive Romberg sign. The pupils reacted normally. When he closed his eyes, he could not open them, as this movement induced a clonus of the eyelids. The clonus of the limbs and head were the same as they had been seven years before. He did not use his eyes for guidance in walking, yet when asked to walk with his eyes closed and helped along, he could not lift his foot from the floor. He had no adiadokokinesis. This test brought out a clonus of the left hand and arm after rotation had gone on for a while. The reflexes were all active, especially on the left side. The clonus looked like the intention tremor seen in Huntington's chorea. Sensation, vibratory sense and the visual fields were normal. The plantar reflex at times caused a Babinski movement on the affected side; the Chaddock reflex did not. The patient's blood pressure varied from systolic 212 and diastolic 116, to systolic 180 and diastolic 126. Urinalysis was negative.

Dr. Rosenbluth considered the clonic movement an automatic afterflow from the lenticular nuclei, which had been started by volition from the cortex or by stimulation resulting from testing the reflex. On account of the defective connections between the affected cortex and these nuclear masses, the usual inhibitory impulses were deficient. Hence these primitive automatic centers in which are patterned the usual habituated functions of the cerebrum, kept going after they had been started, like the runner whose pace continues after crossing the tape despite volition to the contrary.

DISCUSSION

DR. M. NEUSTAEDTER: What are the fundi changes?

DR. ROSENBLUTH: There are none.

DR. LEON T. CORNWALL: Does he experience any subjective phenomena in association with these seizures? Is there any feeling of discomfort?

DR. ROSENBLUTH: No.

DR. C. B. CRAIG: Does he have any spontaneous attacks?

DR. ROSENBLUTH: No. They occur only when the reflexes are tested, or when he is set in motion.

DR. NEUSTAEDTER: Does he complain of pain on that side?

DR. ROSENBLUTH: No.

DR. CRAIG: Do the attacks ever spread from one extremity to include the entire side?

DR. ROSENBLUTH: No. My impression of this phenomenon is that it is probably a dissociation between the cerebral cortex and the striated body due to arteriosclerosis. Naturally if we start the motion, it goes on; it is the type which continues even after the incentive for it has stopped.

A CASE OF NEUROBLASTOMA. PRESENTATION OF PATHOLOGIC SPECIMENS AND LANTERN SLIDES. MAX LEDERER (by invitation).

The patient from which these specimens were obtained was a girl 3 years and 6 months old, who was admitted to the Jewish Hospital of Brooklyn, on Oct. 4, 1924.

The chief complaint was shortness of breath and cough for a year and a half, with a bulging of the left eye, which had been noticed for two months. The past history stated that the child had been suffering from continuous colds since birth, and that in the past year and a half the mother had noticed that the child was short of breath, and that there was edema of both extremities. The family physician reported later that he had discovered an enlarged heart, with a double murmur at the base. He had interpreted this as a syphilitic lesion of the heart, because there was a definite history of syphilis in the grandparents and in the parents. He had treated the child with mercury and iodids, which he thought had resulted in some improvement.

On admission, there was a bulging of the left side of the face, with a left exophthalmos. The heart condition was evident, with what seemed to be signs of pericarditis. A mass was felt in the left hypochondrium, which was thought to be spleen. The child was in the hospital for two months, and was thoroughly studied. The only positive signs were the cardiac condition, the left exophthalmos, and the mass which was thought to be enlarged spleen on the left side. All clinical and pathologic examinations, including repeated Wassermann tests, were negative. The cerebrospinal fluid examinations showed nothing.

Blood counts showed anemia, rather rapidly progressive, and the blood chemistry and urine examinations were negative. Roentgen-ray examinations disclosed at first a rather indefinite kidney shadow on the left side. The kidney was not clearly defined, although the right was plainly visible. In the right femur, there was an area of bone rarefaction and of bone production, which was interpreted as being due to an osteosarcoma. Later, in the calvarium and about the left orbit, areas of rarefaction were noted. It was considered a case of osteosarcoma originating in the right femur, which had metastasized to the skull. The child became progressively worse, and on October 31, developed a definite left-sided facial paralysis. Hearing was not tested. The child died two months after admission to the hospital. The blood pressure during the time in the hospital ranged from systolic 105 and diastolic 75, to systolic 110 and diastolic 70, which is a little high for a child of that age.

At necropsy we found a very large heart and an area of scarring in the left ventricle near the apex, about the size of a silver dollar. This was covered with a tab of fibrous tissue, which caused an adhesion to the parietal pericardium. The left ventricle was tremendously dilated and somewhat hypertrophied. We were at a loss to interpret this finding. We did not know whether it was due to syphilis which may have existed, or to some embolic condition, perhaps coexistent with one of the repeated infections of which the child gave a history. In the left hypochondrium, we found a mass above the left kidney causing pressure atrophy of the upper pole. It was lobulated, with grayish white tissue, some red and some yellow. There were no enlarged lymph nodes in the retroperitoneum. The growth did not involve the kidney itself nor the diaphragm. There were no regional metastases, either by the lymphatics or by contiguity. When one looked at the anterior surface, the cortex of the suprarenal was plainly seen. The chest was absolutely free from any malignancy. In the head, we found that the calvarium was riddled with metastases, from the frontal portion back to the occipital. The dura was also infiltrated, there being a number of metastases along the superior longitudinal sinus and a thrombosis of the longitudinal sinus itself. The thrombus was not malignant. It was a blood platelet and fibrin thrombus. There was a large metastasis over the left occipital lobe, causing a depression in the occipital lobe and some loss of substance and perforation of that lobe, but not into the posterior horn of the ventricle. There were metastases in the dura covering the petrous portion of the left temporal bone, surrounding both seventh and eighth nerves; there was also a large metastasis in the orbit itself, spreading and pushing the eye forward, accounting for the exophthalmos.

This case belongs to that group of neuroblastoma described by Hutchinson. It is strange that the tumors of the left side of the suprarenal metastasize on the left side, causing exophthalmos and cranial metastases, while those on the right side usually do not metastasize to the cranium. These neuroblastomas metastasize only by virtue of the undifferentiated nerve cells, not by virtue of the ganglion cells. Ganglion cells are never found in the metastases. For that reason the metastases can be confused with a sarcoma, and the diagnosis be erroneously made. No rosets were found in this growth. We have here a classical neuroblastoma (except for the absence of rosets), which can be diagnosed clinically. Occasionally, these cases are erroneously diagnosed, particularly when attention is focused on the eye only and when sections are removed from a retro-orbital tumor.

In this case, the child was subjected to intensive antisyphilitic treatment, without the slightest effect. Deep roentgen-ray irradiation was attempted, and

the consensus of opinion of all who attended the child was that the exophthalmos and the swelling of the face diminished somewhat, but of course such treatment was ineffectual.

DISCUSSION

Dr. J. H. Globus: This is another extremely interesting instance added to a fairly large group of cases of neuroblastoma which have been described since the first publications of Marchand, Wright and Martius. They have opened this important chapter on the pathology of tumors of the sympathetic nervous system which is not only interesting to the pathologist, but also is of great service to neurologists. Many authors have followed them, particularly Landau, Wohl, R. A. Lambert, and others, who have studied the question of neuroblastoma and helped to solve the problem. They have rescued this particular form of tumor from the melting pot of sarcoma, and have also established the fact that not all so-called neuroblastomas are neuroblastomas; that is to say, there are various stages or forms of tumors grouped under that name, although they represent different stages in the development of the neuroblast. In my opinion, the tumor shown in this patient is not really a neuroblastoma in the true sense of the word. I believe that there are to be seen in this tumor large cells apparently sympathoblasts, showing already fairly high differentiation, which mark it as a sympathoblastoma. As we were told that the metastasis in this case was limited, involving only the bony structures, it would seem that the tumor did not behave fully as a malignant neuroblastoma. I think I have seen some "rosets" in some of the sections shown. What we are dealing with here is, in my opinion, a tumor belonging to the general group of neuroblastomas, but in this instance the cells have reached a higher stage of differentiation and belong to the stage of the sympathoblast. The lack of widespread metastases, the lesser degree of malignancy and the cellular make-up would mark the tumor as a sympathoblastoma.

Dr. Lederer: I am grateful to Dr. Globus for the view that he has expressed. The case was of much interest to us, and one of the reasons why I called the tumor a neuroblastoma was because Harbitz advised that these tumors be called neuroblastoma without any shadings. The question whether it is a neuroblastoma or a sympathoblastoma is after all academic. What I attempted to do was merely to impress this condition more clearly on the clinician than on the pathologist, because so far as I have been able to learn, a great many of these cases are overlooked. The pathologic condition of the abdomen is lost sight of on account of the pathologic condition that surrounds the eye.

Treatment of Peripheral Nerve Paralysis with Diathermia. A. Lux (by invitation).

At the present stage of our knowledge of electricity, we are convinced that it has no curative influence on a paralyzed nerve, as is commonly believed. Nevertheless, we feel that constant current will increase the irritability of muscle and nerve, and, according to a recent theory, interrupted current will prevent the atrophy of the nerve.

The author has accidentally observed the influence of diathermia on a paralyzed nerve, and has through careful study postulated the various methods in applying this type of current on different parts of the body wherever needed.

More than a hundred patients with paralysis of the peripheral nerve were treated by this method.

The case of a man, aged 26, is demonstrated here as one of the most striking results obtained. This patient was referred to the Montefiore Hospital with the following history:

Sixteen years before, during a mastoid operation, the facial nerve was injured; this resulted in a complete peripheral left facial paralysis. Electricity in all its forms was tried in various institutions, without result. When the patient was examined at the Montefiore Hospital, the following was the status of the case: The face was drawn to the left side; no nasolabial folds were visible on the paralyzed side. When he attempted to whistle or to show his teeth, the typical picture of facial paralysis was seen. The patient could not close his lid at all, and the cornea showed signs of superficial inflammation due to exposure. Sensation of the skin was normal. The patient said that the condition of his face had been the same for the last sixteen years. There was partial reaction of degeneration.

Diathermia was applied according to the usual routine. After five treatments, the patient reported that he felt as though the face were more pliable. After ten treatments, he made the first attempt to close his eye spontaneously. After twenty-four treatments, the face appeared equal on both sides; the nasolabial fold was distinct on both sides; attempts to whistle or show the teeth showed no abnormality. The patient closed his eyelid spontaneously. The electric reaction of facial nerve revealed no difference as compared to the other side of the face.*

The explanation for this unusual case is probably that there was a scar left on the nerve due to the injury, and by concentrating the entire diathermia current on this part, the scar tissue was absorbed. We believe that hyperemia caused by the diathermia current is the effective agent. This hyperemia is different from hyperemias originated by all other methods, because:

1. The current of diathermia penetrates into the deep-seated organ, and produces heat in the organ subject to the treatment.

2. Warmth produced by diathermia is originated by a free energy which is introduced into the body by means of electricity. The warmth produced by all other methods is heat obtained from the organism itself.

3. For the reasons given, diathermia brings a surplus of energy into the diseased tissues, while all other methods cause an increased use of the body's own energy.

DISCUSSION

Dr. G. H. Hyslop: I should like to ask whether Dr. Lux has tried using this form of electricity on patients with organic disease of the spinal cord in the acute stages. In the ward at Bellevue this fall, there was a young boy with multiple sclerosis who had a relapse, and in this relapse developed complete paraplegia with sensory loss, which enabled us to state that he had a large patch in the lower cervical region. After this state of complete paraplegia had been in existence for ten days or two weeks, I had him placed on localized diathermia focused on the level of this presumed patch. It was in the third treatment that the patient observed to the physiotherapy aide that he thought somebody had taken the stockings off his feet, and two weeks following that reaction, the boy was able to stand. The patient was an intelligent boy, and stated that during the application of diathermia he had subjective sensations, paresthesias, at times, as well as an awareness of portions of the body which when examined still were anesthetic. That experience led us to try the same form of treatment in certain other instances. We do not know yet what it

means. We have not had enough material to be able to tell what sort of response may be expected comparable to what is observed in peripheral nerve lesions.

Dr. Smith Ely Jelliffe: Have you had any experience as regards anterior horn involvements (poliomyelitides); and also with reference to syringomyelias? We know that for many years Lhermitte and a number of French observers have been using various types of electrical stimuli over the syringomyelitic areas.

Dr. Globus: I have two academic questions to ask. The first is: What ground have you for supposing and how can you prove that absorption of scar tissue takes place under this method of treatment? Have you had means of observing it in this case? How do you know that there was a scar over the nerve and that such a scar was absorbed by the aid of your treatment? The second question is: How do you know that the application of diathermia from the outside increases metabolism of tissues? How do you know that no metabolic change takes place where diathermia is applied?

Dr. C. B. Craig: Have you tried this treatment with cases of trifacial neuralgia? If so, with what result?

Dr. M. Neustaedter: I should like to know whether you have tried this treatment with peripheral palsies with complete reaction of degeneration, and, if so, what result has been obtained.

Dr. Lux: The observations at Bellevue Hospital are interesting. At the present time, I am treating a great number of patients with those types of cases. In the very beginning of the treatment astonishing results are obtained. I have made that observation in ten patients, particularly if the heat is applied generally instead of on the spot of the lesion. Patients who cannot walk will start to walk, but then they fail. This is most likely the influence of the general hyperemia sent forth by the diathermia which make these changes. I have not been able to observe distinct changes. I am working on ten cases now at the Montefiore Hospital. The results are encouraging only in the beginning, and I have not been able to obtain definite results.

In reply to Dr. Jelliffe's question concerning cases of syringomyelia, treatment is greatly hampered in that type of case by the fact that the people do not perceive the heat. I began treating a couple of patients, but could go no further with them. I am trying to treat patients now with a current which cannot cause burns, but that naturally takes months before we can get results.

In reply to Dr. Craig's question, trifacial neuralgia has been treated by others as well as by myself. Dr. Wolf at Mount Sinai Hospital has treated some of Dr. Abrahamson's patients. Our method is to treat the patient through the eyes. Good results have seldom been obtained by treating the nerve itself, but we have had encouraging results with the other method, even in cases in which no other form of treatment has benefited the patient.

In answer to Dr. Globus, I pointed out in my paper that there was possibly scar tissue in the facial nerve. He may be right; there may have been no scar tissue, but there was a lesion in the nerve. We have propagated regeneration of the nerve. The absorption of scar tissue can be easily proved from experiments in animals. I have pictures which I made in Paris showing animals with scar tissue in the peripheral nerves, and how it was absorbed.

In regard to the question about the heat and metabolism in diathermia: The patient has a sensation of heat in the skin. By applying diathermia, the patient feels heat inside, and the skin warms up later. If you apply 300 volts,

the patient will feel heat inside, and if you stop the current, you see no effect on the skin. Diathermia heats up the particular part on the principle of resistance, just as an electric iron will heat up the body. It propagates hyperemia of the skin, and encourages the superficial tissues for a chemical interchange. I pointed out the chemical interchange in my paper, and I mentioned metabolism as a side track, which has not been proved, but the chemical interchange has been proved by numerous experiments.

ADDRESS OF THE PRESIDENT-ELECT OF THE SOCIETY. DR. I. ABRAHAMSON.

I have no words in which to make acknowledgment of the great honor you have done me.

For many years, neurology has been winning its way upward in the hierarchy of medical sciences, until now its position is assured, and all pay tribute to it as the science of the executive and administrative and legislative departments of the confederacy of functions that constitute human life. Particular aspects of our constitutional habit interest each of us, and excite us, according to our nature and our opportunities, to investigate them. Dr. Jelliffe will elucidate for you the impulse that determines your choice of interest, and he will also warn you of the penalties that will confront you and cause a complex if that impulse should be denied expression. I should like to add to his weighty warnings my most earnest request that you give free vent to that expression here. The psychic health of this Society depends on that free expression, in written or in spoken speech. The Society expects and will appreciate a communication from every one of its Fellows, and in favoring us with their communications, the Fellows will find that their complexes will cease from troubling, and their motor equivalents will find rest.

My nature and opportunities have been such that I have found myself intrigued mainly by motor equivalents. I happened to be placed near the center of the epidemics of epidemic (lethargic) encephalitis in this country, and was in consequence led to study the motor manifestations of this disease as I saw them, and to report the results to you. This, in turn, caused me to be curious about the motor mechanism, and at various times I have submitted for your criticism, deductions and inferences as to the nature of muscular action, which clinical study of this epidemic disease seemed to justify. I shall summarize briefly what we think we know of some common motor actions and their causes in the hope that certain among you may be led to concern yourselves to check up the work already done, to correct it where it is at fault, and by your observations to carry it forward from the point of abstract interest where it now halts to the point where it may become available for relieving the suffering it causes.

The function of mobility of the body and of its several parts is carried out by an organ which we call the musculature, which is composed of an infinite number of muscular units, grouped to initiate, to reinforce, to maintain, to balance, to stop, or to reverse such changes in our skeletal attitude as we consciously desire or emotionally suffer. A vast and complex nervous mechanism controls the musculature, and produces in it the phasic changes which tend to voluntary movement. These changes are caused by chemical action in the muscle cells, that give rise to increase or lowering of what we call muscle tone. As evidence of the chemical changes, we have reports of careful workers on the metabolism of active and of resting muscles. Such chemical changes are accompanied by electrical changes of measurable direction and extent; also by other physical changes, among which we for the moment are chiefly concerned with the elastic state of contraction or tone of the examined muscles.

If we consider the arm hanging quietly by the side, we may without serious fault regard the tone of the flexors of the elbow in that position as on a par with the tone of the extensors. The arm hangs quietly, the flexors do not dominate over the tone of their antagonists, the extensors, and no movement results. If the flexor tone does dominate, the arm bends upward. The flexors shorten, the extensors stretch, and as the movement progresses, through a series of intermediate postures to the desired posture, to every new posture there pertains a definite enhancement of muscle tone in the flexors and a definite diminution of muscle tone in the extensors.

Throughout the movement, this enhancement of tone in the flexors takes place at a definite rate. And each serial posture must be maintained until that of its successor in the movement can be superimposed, to produce the smooth, thrifty character that denotes normal movement.

Normally, the tone changes follow one another at a rate of about twenty per second, and each change at that rate is ample in extent and in duration to fulfil its desired end. We have not yet attained much exactness in determining the amplitude of the individual changes. The amount of the successive changes of tone may vary rhythmically or arrhythmically.

The duration of the individual changes may vary, too, and so may the rate at which they follow one another, either with or without variation in the extent or duration of the individual changes. We have therefore at least three variables to consider in the changes of tone in the flexor muscles, namely, the extent of intensity of each change of tone, its duration and the rate at which the changes occur.

These three variables which we distinguish in the enhancement of the tone of the flexors we can likewise distinguish in the synchronous diminution of tone in the extensors. When we are confronted with a defect in voluntary movement, we try to determine by analysis of the defect just where the fault lies among these variables.

Boers attributes the tremor of old age mainly to hypotonia, to the inadequacy of the intensity of the successive changes in tone, the inadequacy both of the enhancement of the tone of the agonists and the diminution of tone in the antagonists. It seems unlikely that other things being equal, such inadequacy would create much disorder in movement. Rather should it show itself in delay and limitation and weakness of the movement. Von Monakow regards the tremor of Parkinson's disease as partly due to hypotonia, but partly also to a falling off in the rate of succession of the changes in tone. He observed that the rate in Parkinson's disease fell from 20 to 16 per second, and inferred that between the changes the muscles had time to relax in part, which gave the movement an uncertain and oscillatory character. If the hypotonia and the falling off in the rate of change be equal in both, the agonists and antagonists, it would seem, *a priori*, as if the movement would be less disorderly than if these faults affected one group to a greater degree than the other. And the greatest likelihood of disturbance seems to lie, not in lack of intensity or even in diminution of frequency, but in lack of correspondence between the duration of the enhancement of tone in the agonists and of the reduction of tone in the antagonists.

Our studies so far have been mainly concerned with the tone enhancement changes. We do not as yet know much about the complemental reduction of tone in the antagonists. But if, as I am inclined to think, the enhancement of tone in a muscle is normally in part a liberation of energy due to the cessation of prevailing inhibitory reflex nervous action and diminution of tone in the antagonists is due to an increased activity of such inhibitory action, we

shall find the key to many of these problems of disorderly movement, not in a study of the more or less passively contracting agonist, but in the study of the active inhibition of tone that is simultaneously induced in the antagonists.

The prevailing tone of muscles, the tone, so to speak, of each particular muscle locality, is maintained in part at least by the sarcoplasmatic portion of voluntary muscle. The sarcoplasmatic portion of voluntary muscle is distinguished from the fibrillar portion by histologic structure, chemical composition, electrical reaction, function and nerve supply. The nerve supply is derived from neurons which originate in cells in the lateral horn of the spinal cord and their analogues in the cerebral end of the nerve axis. It is noteworthy that epinephrin which produces fine tremors in normal persons, and emotion, exertion, or excitement, which stimulate secretion of epinephrin and also induce tremulousness, all aggravate the tremor of Parkinson's disease. This positive result may be attributable to stimulation of the active inhibition of tone in the antagonist groups, whose nerve supply is closely related to the sympathetic system of nerves that epinephrin excites.

On these prevailing local tone changes which I am suggesting are established at this neurochemical level the voluntary phasic changes of the musculature as a whole, which are superimposed and correlated by reflex nervous action. This reflex nervous action is of such complexity that I think I may make the matter clearer by turning from the elastic state of the contracting voluntary muscles to the mechanism by which the influence of the will is brought to bear on them.

The desire that evokes a movement calls forth as one of its essential attributes a series of postural images, linking the desired with the existing posture. Each postural image has a certain intensity with which it demands motor expression and which leads it to dominate over the existing postural images so that it effectively prevails. These postural images leave the conceptual sphere, and pass in regular order with a given urgency into a prepyramidal region of basal nuclei and associated structures, where they lose their conceptual character and become converted into nerve impulses which ultimately pass to the cells of the rolandic areas. In their passage, these impulses are finally analyzed and distributed along specific neurons according to the ultimate destination of the impulses they carry. In other words, even in the prepyramidal region, there is definite functional localization. And when irritative lesions affect these prepyramidal neurons we see the spontaneous muscle twitchings of myoclonus, or in degenerative lesions, dystonia.

We have no means of estimating the intensity, rate and frequency of the postural images that excite the prepyramidal structures. But the movements which express each of these successive postural images receive in this region their tone qualities. It is here that the movement acquires its readiness, its strength, its rhythm and its integration with the existing state of the musculature. Here again the enhancement of tone is normally in part a liberation of energy due to the cessation of the generally prevailing inhibition of reflex and automatic and emotional nervous action, and the complemental diminution of tone in the muscles that oppose the muscular expression is due to an increased action of the prevailing inhibitory influences.

From the prepyramidal region, the impulses pass in ordered sequence to the cells of the rolandic area, whence at regular intervals they are discharged through the pyramidal tract to the anterior horn cell, and thence by the lower motor neuron to the voluntary muscle.

In the conceptual sphere, variations in the intensity, rate and frequency of the excited postural images can produce chaos in movement, but every

movement expresses a purposeful posture and not an isolated muscular act. It is chiefly in this sphere that the choreiform movements originate.

Every willed movement has a definite aim; it fulfils to the satisfaction of the critique the desire which evoked the movement. That desire called forth as one of its essential attributes a series of central after-images of the postures linking the desired with the existing posture. And every component posture of the willed movement, as the movement was performed, excited a peripheral after-image of the moving part. Those postural images that were initiated by the desire and those that were excited peripherally by its performance neutralize one another perfectly, satisfy the critique, and the desired aim being achieved, the musculature comes to rest or proceeds to express desires anew.

In chorea, the neutralization does not occur; the central motor images remain undischarged and capable of exciting further muscular movement. The peripheral after-image of the choreiform movement has also the power to excite change, as it induces a desire to correct its motor consequences. Further movements ensue, and each posture achieved contributes further to disturb the postural associations until they become a whirl of futility and confusion. So fatigue comes, and adds to the postural instability. And the reproduced postures succeed one another in increasingly chaotic sequence and with uncalled for violence. The movements no longer express conscious desire, but are expressive merely of the dominant postural images that emerge from the emotional, volitional, and peripheral excitations that are rioting through the sphere of the postural associations, exciting one muscular posture after another. And as these are not harmonized with their predecessors, but merely supplant them, they lack tone, for they possess only the surplus tone of their dominance.

A still greater tone lack is observable in the usual affections of the prepyramidal system, but here we see defects in the several qualities of tone. affections of the readiness, strength, rhythm and duration of the movement. There may be the myoclonus or dystonia that we have already mentioned, but these I think occur as the result of affections near the end of the prepyramidal system, where it is converging on the rolandic area. Usually, we see a more diffuse increase or lack of muscle tone. There may be a mild paresis, or delayed initiation and retarded execution of movement, or diminished volume and extent of the movement, or easy fatigability, or loss of physiologically associated movements or lack of affective movement. These changes result in alterations in station and in gait, disturbances in the higher automatic coordinations, such as walking, chewing, swallowing, and speaking adiadokokinesis and propulsive movements.

When we come to the lesions of the pyramidal tract itself, we find the phasic variation of tone more or less abolished, together with all the attributes of plasticity that cerebral inhibition of tone confers. There is loss of movement, increased resistance to passive movements, rigidity, with clonuses and exaggerated deep reflexes, and return of the primitive skin reflexes, such as the Babinski reflex. If some movement survives, the pull of the antagonist sets in earlier and persists longer, so that its recoil effect is premature and excessive.

The rigid muscles assume fixed attitudes which reflect mainly the primitive dominance of the local flexor tone over the extensor tone. The force of gravity is too feeble to modify these fixed attitudes, but sleep usually relaxes them.

And if the affected members are not rendered immobile, unsupported they display a coarse tremor, affect the extremities more than the head, the forearm and wrist more than the hand, the leg and ankle more than the toes. It is coarser and more irregular than the typical parkinsonian tremor. This tremor reaches its height when the rigidity scarcely suffices to limit the range of movement. It is always preceded by rigidity, and disappears when the rigidity suffices to immobilize.

The three tone variables, the extent or intensity, the duration and the frequency of the enhancement or diminution of the elastic state of contraction in muscle, we have considered at the lowest or neurochemical level; and we have briefly sketched the course of the alterations in these variables from the psychic level. I think the plastic changes in the musculature arise from a liberation of energy due to cessation of preexisting nervous inhibition of tone when the tone is enhanced, and to a conservation of energy due to increase of preexisting nervous inhibition when the tone is diminished. The prevailing local tone of any muscular area is a vegetative function. The prevailing general tone of the whole musculature is largely determined by the mental state, by the existing affective condition, of which the desired posture is merely one muscular expression. We have been slow to realize the vegetative quality of the muscular organ, and we have been still more reluctant to consider movement as an emotional expression. I have therefore ventured to give this brief sketch of motor actions and reactions, in the hope that your observations will fill in the obvious gaps in our knowledge of muscular action, and will clear up what is still mysterious about the wondrous ways in which men move in health and in disease.

Book Reviews

THE MEDICAL SCIENCES IN THE GERMAN UNIVERSITIES. A STUDY IN THE HISTORY OF CIVILIZATION. TRANSLATED FROM THE GERMAN OF THEODOR BILLROTH WITH AN INTRODUCTION BY WILLIAM H. WELCH. Pp. 292. New York: The Macmillan Company.

We quote in a disjointed way from Dr. Welch's introduction:

"That a book on medical education published nearly fifty years ago should appear now for the first time in English translation may seem to demand an explanation." "Here is a work of enduring value, characterized by a breadth of view and enunciation of certain general principles as sound and as needful of utterance today as when they were first expressed; a book, moreover, singularly suggestive and stimulating in its discussion of many fundamental as well as detailed problems of medical education, which are still of vital interest, especially in this country at the present stage of development of our medical schools." "No one better qualified by training and experience has written upon the subject." "Billroth combined in unusual measure scientific and practical interests."

"The pages of this book will afford, even in translation, abundant evidence of Billroth's literary gifts, his vigor of expression, his epigrammatic wit, his clear and logical thinking, his historical sense, his practical wisdom and hold on reality, his thorough command of his subject, his courage and independence of thought and utterance without regard to consequences, and his devotion to truth."

These brief excerpts will indicate that this unusual book will be of great interest and value to all interested in the history of medicine, medical education, the relation of the medical man to the public, the interrelation of professor and student and cognate subjects.

INTERNATIONAL CLINICS. Edited by HENRY W. CATTELL, A.M., M.D., Philadelphia, Pa., with the collaboration of CHARLES H. MAYO, M.D. Volume I. Thirty-Fifth Series. Pp. 294. Philadelphia: J. B. Lippincott Company, 1925.

This volume contains more than usual of interest to the neuropsychiatrist.

L. F. Barker has an hour's excellent talk, clear and reasonable, on the treatment of the psychoneuroses and the milder forms of the major psychoses. Naturally, this lecture is designed for the general practitioner and should be most helpful.

The lecture of C. Judson Herrick on some relationships of the visceral nervous system is more technical, but the fundamentals of structure and function are so lucidly presented that the talk is not only of value to neurologists but may easily be grasped by any doctor or medical student. The much disputed subject of the synapse is clarified, with conclusions that may be drawn from the anatomic findings.

The principles of visceral control are clearly stated, and the partial control of voluntary muscles by way of the sympathetic system is also discussed.

James Burnet of Edinburgh reports a case of exophthalmic goiter in a child, aged 9 years, with a brief discussion of the subject.

Remarks on the psychology of paranoia are contributed by Edouard Rétif, a physician on the staff of the insane asylum of the Department of the Rhone.

His thesis is to the effect that the delusions of paranoia arise from the emergence of the primitive ego. He adopts the idea of William James that there are essentially two egos, the primitive and the social. Under certain circumstances, the primitive as opposed to the social ego, becomes integrally restored. It is one of the tests of psychology to determine what these circumstances are. The author states that two of these circumstances are play and revery, the former being "nothing but an objective revery." In a preponderating majority of either, the contents are ideas of grandeur. Affective logic is primitive logic and "return to this kind of primitive logic is insanity." The author then discusses in an interesting way the mechanism of the production of the paranoid delusions of different types, all of which have an affective basis.

Evidently this article was written in French, and the translation is only fairly well done. For instance, délire is translated delirium instead of delusion.

Ralph C. Hamill contributes a paper on amnesia and pathologic stealing based on an interesting and instructive case. The patient was a man, aged 32, whose peculations were based on boyhood antagonism to his father. The amnesia with fugues was a means of escape from an uneasy conscience and other consequences of his thefts. In the analysis, principally by way of dreams, the patient himself arrived at the explanation, and as this became clearer, memory of the amnesic period returned. The inference is that his future conduct would be better.

A short paper on psychoneuroses in relation to general medicine by Alfred Gordon deals with the unfounded fears and worries of neurotic patients, and the futility of considering such symptoms as caused by organic disease.

The remainder of the volume is good.

TUMORS OF THE SPINAL CORD. THE SYMPTOMS OF IRRITATION AND COMPRESSION OF THE SPINAL CORD AND NERVE ROOTS. PATHOLOGY, SYMPTOMATOLOGY, DIAGNOSIS AND TREATMENT. By CHARLES A. ELSBERG, M.D., with Three Hundred and Fifty-Four Illustrations. Pp. 408. New York: Paul B. Hoeber, 1925. Price $10.00.

This is an excellent, complete and up-to-date treatise. The arrangement is rather unusual, probably because the work is essentially personal and is largely composed of a number of addresses and lectures by the author "covering the last ten years." A study of eighty-one cases of spinal cord tumors observed by Dr. Elsberg during a period of twelve years forms the basis of the book.

After a brief but adequate historical introduction and three pages on etiology and incidence, 230 pages are devoted to case reports, these being divided into extramedullary tumors (fifty-four cases) extradural tumors (fourteen cases) and intramedullary tumors (thirteen cases). Of the extramedullary growths, those of the conus and cauda equina (twelve cases) are considered as a subgroup. Most of the cases are reported in considerable detail, including results of operation, with numerous diagrams of sensory symptoms, and photographs and photomicrographs. These reports constitute a rich mine of clinical information, but this has to be dug out by painstaking reading. In fact, throughout this carefully prepared book, one misses the useful summary, a statement of the lesson to be taught or learned, and the conclusions to be drawn from the mass of facts presented.

Chapter VII (eleven pages) is on the location of cord tumors and their mechanical effects, and Chapter VIII (nine pages) on the cerebrospinal fluid in its relation to tumors of the cord. Chapter IX (ten pages) covers sub-

jective (sensory) and early motor symptoms, Chapter X (ten pages and rather inadequate) motor reflex and trophic disturbances and Chapter XI (fourteen pages) symptomatology, meaning thereby "objective sensory disturbances; the Brown-Séquard syndrome and its variations." In Chapter XII (twelve pages) are presented "the clinical features at different levels," and Chapter XIII (fourteen pages) is on the pathologic anatomy of these tumors. As the number of pages indicates, neither is exhaustive. Chapter XIV (seven pages), largely pictures, embraces a few remarks on multiple tumors, recurrence after removal, metastases and irremovable growths.

Chapter XV (nineteen pages) on diagnosis, including general diagnosis, regional diagnosis and differential diagnosis, is a very good textbook article, but from the neurologic standpoint is hardly up to the highest standards. Perhaps the one rarely used procedure of value properly emphasized is examination for symptoms of compression before and after lumbar puncture.

The chapter on treatment needs no comment here; that on results is extremely valuable, obviously being an honest statement of just what was attained in the unusually extensive experience of an unusually skilful surgeon.

A bibliography of 304 numbers, an index of authors and a good index of subjects close the book. Paper and print are good, and the illustrations are unexcelled.

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